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FILE LAST UPDATED: 19 Sep 2007  (20070919/ED)

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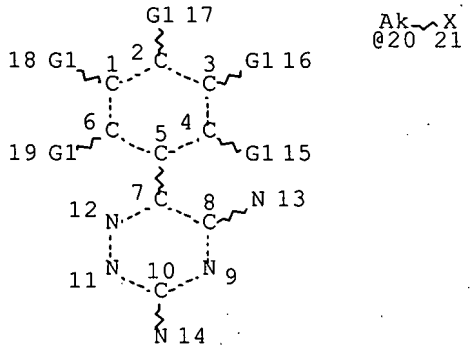


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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  21

STEREO ATTRIBUTES: NONE
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L6            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  84057-84-1
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SCHULWITZ PAUL

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L20           3 SEA FILE=CAPLUS ABB=ON  PLU=ON  L11 AND L19
L21          72 SEA FILE=CAPLUS ABB=ON  PLU=ON  L11 OR L20


=> d l21 ibib abs hitstr tot

L21  ANSWER 1 OF 72  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:710604  CAPLUS  Full-text
DOCUMENT NUMBER:          147:235202
TITLE:                    Process for the preparation of lamotrigine via
                          cyclization of oxodichlorophenylacetamidine
INVENTOR(S):              Garaczi, Sandor; Gegoe, Csaba Lehel; Lukacs, Ferenc;
                          Mate, Attila Gergely; Nyerges, Miklos; Ondi, Levente;
                          Schneider, Geza
PATENT ASSIGNEE(S):       Cf Pharma Gyogyszergyarto Kft., Hung.; Helm AG
SOURCE:                   Hung. Pat. Appl., 21pp.
                          CODEN: HUXXCV
DOCUMENT TYPE:            Patent
LANGUAGE:                 Hungarian
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    ---------------------    --------
     HU 200103073          A2    20030428    HU 2001-3073             20010726 <--
     HU 224026             B1    20050530
PRIORITY APPLN. INFO.:                       HU 2001-3073             20010726 <--
GI
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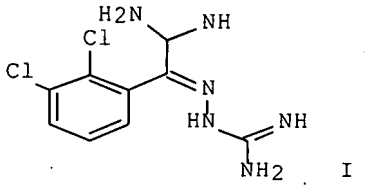


I

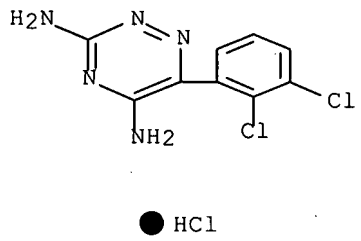
AB The subject of the invention is a process for the preparation of lamotrigine, i.e. 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine, via cyclization of oxodichlorophenylacetamide aminoguanidinohydrazine I.2HCl and the intermediate

products used in this process as well as their salts. According to the invention, the lamotrigine prepared with the process is suitable for the preparation of different pharmaceutical compns., in which case the pharmaceutically acceptable salts of lamotrigine are used.

IT 493025-05-1P, Lamotrigine hydrochloride
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of lamotrigine via cyclization of oxodichlorophenylacetamidine aminoguanidinohydrazine)

RN 493025-05-1 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)-, hydrochloride (1:1) (CA INDEX NAME)



L21 ANSWER 2 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:564587 CAPLUS Full-text

DOCUMENT NUMBER: 143:83487

TITLE: Pharmaceutical combinations with increased sodium channel blocking effects

INVENTOR(S): Kocsis, Pal; Tarnawa, Istvan; Than, Marta; Tihanyi, Karoly; Nemeth, Gyoergy

PATENT ASSIGNEE(S): Richter Gedeon Vegyeszeti Gyar Rt., Hung.

SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005058363	A2	20050630	WO 2004-HU123	20041218 <--
WO 2005058363	A3	20060720		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
HU 200304095	A2	20050728	HU 2003-4095	20031219 <--
AU 2004298911	A1	20050630	AU 2004-298911	20041218 <--

CA 2556342	A1	20050630	CA 2004-2556342		20041218 <--
EP 1699489	A2	20060913	EP 2004-806280		20041218 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU					
CN 1917864	A	20070221	CN 2004-80041830		20041218 <--
KR 2007007040	A	20070112	KR 2006-713930		20060711 <--
IN 2006KN01961	A	20070518	IN 2006-KN1961		20060712 <--
US 2007129370	A1	20070607	US 2006-584661		20060919 <--
PRIORITY APPLN. INFO.:			HU 2003-4095	A	20031219 <--
			WO 2004-HU123	W	20041218

AB The invention relates to novel pharmaceutical combinations with improved sodium channel blocking effect. Further, the invention relates to the use of said pharmaceutical combinations in chronic pain, in disturbances of the motor system, in epilepsy, as well as in other therapeutic fields where the use of sodium channel blockers is acceptable. Serotonin uptake inhibitors potentiated the effect of antiepileptics with sodium channel blocking mechanism of action. Thus, the combined use of the two substances resulted in a more potent pharmaceutical having a more favorable side effect profile.

IT 855519-59-4 855519-61-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical combinations with increased sodium channel blocking effects)

RN 855519-59-4 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)-, mixt. with N-methyl-γ-[4-(trifluoromethyl)phenoxy]benzenepropanamine (9CI) (CA INDEX NAME)

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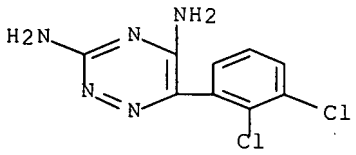
CRN 84057-84-1
CMF C9 H7 Cl2 N5



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CRN 54910-89-3
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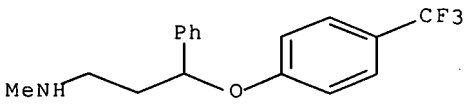

RN 855519-61-8 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)-, mixt. with (1S,4S)-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-N-methyl-1-naphthalenamine (9CI) (CA INDEX NAME)

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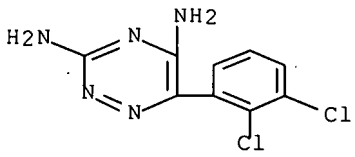
CRN 84057-84-1
CMF C9 H7 Cl2 N5



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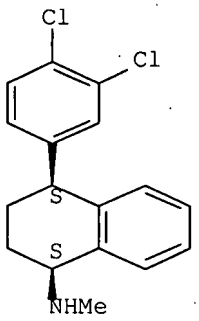
CRN 79617-96-2
CMF C17 H17 Cl2 N

Absolute stereochemistry. Rotation (+).



L21 ANSWER 3 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:421470 CAPLUS Full-text
DOCUMENT NUMBER: 141:7119
TITLE: Preparation of crystalline lamotrigine and its monohydrate
INVENTOR(S): Manjunatha, Sulur G.; Kulkarni, Ashok Krishna; Kishore, Charugundia; Bokka, Ravisankar
PATENT ASSIGNEE(S): Jubilant Organosys Limited, India
SOURCE: Brit. UK Pat. Appl., 25 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

GB 2395483	A	20040526	GB 2003-15608	20030703 <--
WO 2005003104	A2	20050113	WO 2004-IN186	20040628 <--
WO 2005003104	A3	20050922		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2003-15608 A 20030703 <--

OTHER SOURCE(S): CASREACT 141:7119

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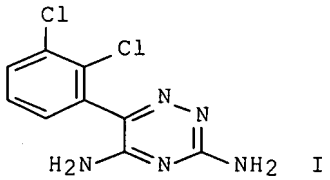


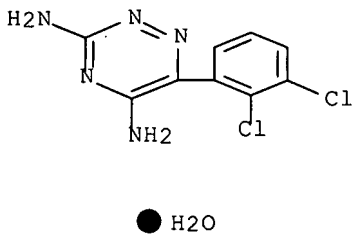
I

AB The invention relates to crystalline lamotrigine (3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine) (I) monohydrate and anhydrous lamotrigine. An improved process for manufacturing these products comprises reacting 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in aqueous mineral acid, optionally together with a water miscible organic solvent, at 30-80° to produce the 2-(2,3-dichlorophenyl)-2- (guanidinylimino)acetonitrile (Schiff base) (II). The Schiff base II is further cyclized in aqueous organic solvent, e.g. alc. to produce pure lamotrigine of a pharmaceutically acceptable quality which on further drying at 45-50° under vacuum yields lamotrigine monohydrate, and/or on further drying at 100-110° yields anhydrous lamotrigine. The lamotrigine monohydrate or anhydrous lamotrigine thereby produced may then be brought into association with a pharmaceutically acceptable carrier for administration to a patient in need thereof.

IT 375347-20-9P, Lamotrigine monohydrate
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(X-ray diffraction anal.; preparation of crystalline lamotrigine and its monohydrate by condensation of 2,3-dichlorobenzoyl cyanide with aminoguanidine and cyclization)

RN 375347-20-9 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)-, monohydrate (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

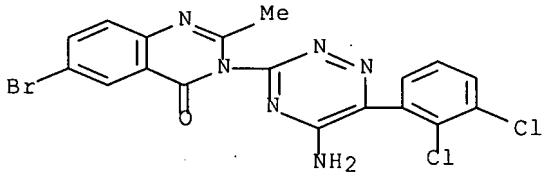
L21 ANSWER 4 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:745740 CAPLUS Full-text
DOCUMENT NUMBER: 140:163810
TITLE: Synthesis, antiviral and cytotoxic activity of 6-bromo-2,3-disubstituted-4(3H)-quinazolinones
AUTHOR(S): Dinakaran, Murugesan; Selvam, Periyaswamy; DeClerco, Erik; Sridhar, Seshaiah Krishnan
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, Periyar College of Pharmaceutical Science, Tiruchirappalli, 620021, India
SOURCE: Biological & Pharmaceutical Bulletin (2003), 26(9), 1278-1282
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:163810

AB In the present study, a series of 6-bromo-2,3-disubstituted-4(3H)-quinazolinones was synthesized by condensation of 6-bromo-2-substituted-benzoxazin-4-one with trimethoprim, pyrimethamine and lamotrigine. The chemical structures of the synthesized compds. were confirmed by means of IR, 1H-NMR and mass spectral and elemental anal. The antiviral activity and cytotoxicity of the compds. were tested in E6SM (Herpes simplex-1 KOS, Herpes simplex-1 TK-KOS ACV, Herpes simplex-2 G, Vaccinia virus; Vesicular stomatitis virus, Parainfluenza-3 virus, Reovirus-1, Sindbis virus, Coxsackie virus B4 and Punta Toro virus) and HeLa cell culture (Vesicular stomatitis virus, Coxsackie virus B4 and Respiratory syncyticla virus). Investigation of anti-HIV activity was done against replication of HIV-1 (HTLV-III B LAI) in MT-4 cells. 6-Bromo-2-phenyl-3-[4-amino-5-(4- chlorophenyl)-6-ethylpyrimidin-2-yl]-4(3H)-quinazolinone (I) exhibited the most potent antiviral activity with a MIC of 1.92 μg/mL against vaccinia virus in E6SM cell culture. The other compds. did not exhibit antiviral activity nor afford significant cytoprotection to the E6SM and HeLa cell culture when challenged with the viruses. The study implies that I may possess activity against Pox viruses including variola. In the anti-HIV study, 6-bromo-2-methyl-3-[4-amino-5-(4-chlorophenyl)-6- ethylpyrimidin-2-yl]-4(3H)-quinazolinone and 6-bromo-2-phenyl-3-[4-amino-5- (4-chlorophenyl)-6-ethylpyrimidin-2-yl]-4(3H)-quinazolinone I exhibited the least cytotoxic concentration (0.424, 0.461 μg/mL) which is an index of the infective viability of mock infected MT-4 cells with HIV-1. None of the compds. exhibited significant anti-HIV activity.

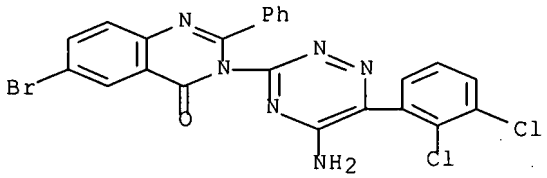
IT 654641-98-2P 654641-99-3P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(preparation, antiviral, and cytotoxic activity of 6-bromo-2,3-disubstituted-
4(3H)-quinazolinones by condensation of 6-bromo-2-substituted-benzoxazin-4-one with trimethoprim, pyrimethamine, and lamotrigine)

RN 654641-98-2 CAPLUS
CN 4(3H)-Quinazolinone, 3-[5-amino-6-(2,3-dichlorophenyl)-1,2,4-triazin-3-yl]-6-bromo-2-methyl- (9CI) (CA INDEX NAME)



RN 654641-99-3 CAPLUS
CN 4(3H)-Quinazolinone, 3-[5-amino-6-(2,3-dichlorophenyl)-1,2,4-triazin-3-yl]-6-bromo-2-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 5 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:507707 CAPLUS Full-text
DOCUMENT NUMBER: 139:69292
TITLE: Process for the preparation of lamotrigine and related 3,5-diamino-6-substituted-1,2,4-triazines via cyclization of cyanoiminoguanidines.
INVENTOR(S): Guntoori, Bhaskar Reddy; Che, Daqing; Murthy, K. S. Keshava
PATENT ASSIGNEE(S): Brantford Chemicals Inc., Can.
SOURCE: U.S., 11 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6586593	B1	20030701	US 2002-46383	20020116 <--
CA 2366521	A1	20030624	CA 2001-2366521	20011224 <--
CA 2366521	C	20070306		

WO 2003078407	A1	20030925	WO 2002-CA1926	20021218 <--
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AU 2002367765	A1	20030929	AU 2002-367765	20021218 <--
EP 1458692	A1	20040922	EP 2002-807048	20021218 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
NZ 533734	A	20051223	NZ 2002-533734	20021218 <--
MX 2004PA06216	A	20050331	MX 2004-PA6216	20040623 <--
IN 2004DN01892	A	20070406	IN 2004-DN1892	20040701 <--
PRIORITY APPLN. INFO.:			CA 2001-2366521 A	20011224 <--
			WO 2002-CA1926 W	20021218 <--

OTHER SOURCE(S): CASREACT 139:69292; MARPAT 139:69292

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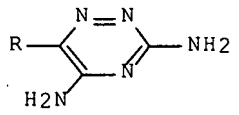


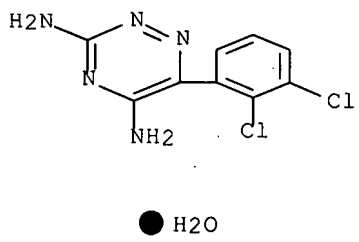
I

AB Title compds. [I; R = (substituted) alkyl, aryl], were prepared by reaction of RCOCN with aminoguanidine in the presence of an organic sulfonic acid in an organic solvent under anhydrous conditions to give (HO)C(R)(CN)NHNC(NH2)2, dehydration of this to give NCC(R)[:NN:C(NH2)2], and cyclization of the latter. Thus, aminoguanidine hydrochloride in DMF was treated with MeSO3H and 2,3-dichlorobenzoyl chloride followed by stirring for 1 h, addition of SOCl2, and stirring for 1 h to give 39.2% iminoguanidine derivative The latter was refluxed with KOH in Me2CHOH to give 82% lamotrigine monohydrate.

IT 375347-20-9P, Lamotrigine hydrate
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for the preparation of lamotrigine and related 3,5-diamino-6-substituted-1,2,4-triazines via cyclization of cyanoiminoguanidines)

RN 375347-20-9 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)-, monohydrate (9CI) (CA INDEX NAME)



● H2O

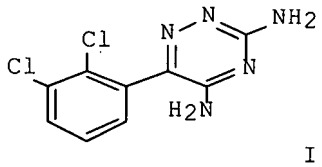
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 6 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:76761 CAPLUS Full-text
DOCUMENT NUMBER: 138:137336
TITLE: Method for producing lamotrigine from alpha-oxo-2,3-dichlorophenylacetamidinoaminoguanidino hydrazone by ring closure reaction
INVENTOR(S): Schneider, Geza; Gegoe, Csaba Lehel; Ondi, Levente; Mate, Attila Gergely; Lukacs, Ferenc; Nyerges, Miklos; Garaczi, Sandor
PATENT ASSIGNEE(S): Helm AG, Germany; CF Pharma Gyogyszergyarto Kft.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008393	A1	20030130	WO 2002-EP7433	20020704 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10134980	A1	20030213	DE 2001-10134980	20010717 <--
DE 10134980	C2	20030528		
CA 2417435	A1	20030130	CA 2002-2417435	20020704 <--
CA 2417435	C	20040113		
AU 2002325297	A1	20030303	AU 2002-325297	20020704 <--
EP 1311492	A1	20030521	EP 2002-758308	20020704 <--
EP 1311492	B1	20040908		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, BG, CZ, EE				
ES 2224074	T3	20050301	ES 2002-2758308	20020704 <--
US 2003191310	A1	20031009	US 2003-343225	20030515 <--
US 6683182	B2	20040127		

PRIORITY APPLN. INFO.: DE 2001-10134980 A 20010717 <--
WO 2002-EP7433 W 20020704 <--

OTHER SOURCE(S): CASREACT 138:137336; MARPAT 138:137336
GI



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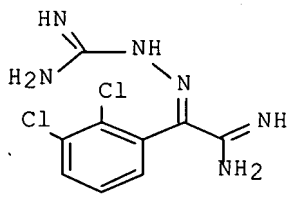

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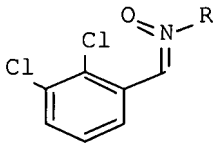


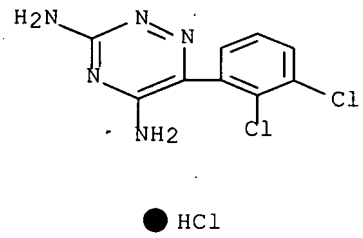
III

AB The invention relates to a method for producing 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine [lamotrigine (I)], or its pharmaceutically acceptable salts, by ring closure reaction from α-oxo-2,3-dichlorophenylacetamidinoaminoguanidino hydrazone (II) or its salts. The preparation of II from N-oxides, III [R = linear, branched or cyclic (un)substituted alkyl, aryl, aralkyl], or their salts, are also described. Thus, I was prepared from 2,3-Cl2C6H3CH:N(O)Ph, via cyanation with NaCN, amination to the acetamidine hydrochloride, reaction with aminoguanine bicarbonate to give II·HCl, treatment with aqueous NaOH to give the free base, which is cyclized to I; cyclization of II·HCl gives I·HCl.

IT 493025-05-1P, Lamotrigine hydrochloride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of lamotrigine from α-oxo-2,3-dichlorophenylacetamidinoaminoguanidino hydrazone by a ring closure reaction)

RN 493025-05-1 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 7 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:933006 CAPLUS Full-text
DOCUMENT NUMBER: 139:122536
TITLE: Influence of administration vehicles and drug formulations on the pharmacokinetic profile of lamotrigine in rats
AUTHOR(S): Castel-Branco, M. M.; Figueiredo, I. V.; Falcao, A. C.; Macedo, T. R. A.; Caramona, M. M.
CORPORATE SOURCE: Laboratory of Pharmacology, Faculty of Pharmacy, Coimbra University, Coimbra, Port.
SOURCE: Fundamental & Clinical Pharmacology (2002), 16(5), 331-336
CODEN: FCPHEZ; ISSN: 0767-3981
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

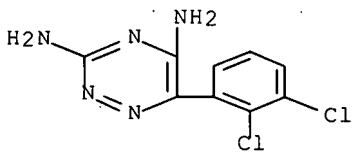
AB Given that administration vehicles and drug formulations can affect drug bioavailability, their influence on the pharmacokinetic profile of lamotrigine (LTG), a new-generation anti-epileptic drug, was studied in rats. Three different formulations administered i.p. at a dose of 10 mg/kg were used: (1) LTG suspended in a 0.25% methylcellulose solution (2) LTG dissolved in a 50% propylene glycol solution, and (3) LTG isethionate dissolved in distilled water. Plasma and brain homogenate levels were determined in order to evaluate vehicle-dependent drug absorption. The results demonstrated rapid absorption of LTG when it was administered as an aqueous solution, in contrast to a slower and more erratic absorption after the injection of either the lipophilic solution or the suspension. A plasma peak was achieved 15 min post-dose with the aqueous solution, with a brain peak being achieved 15 min later, while with the other formulations both plasma and brain homogenate peaks were reached 2 h after LTG administration. This study suggests that LTG isethionate dissolved in distilled water is the most suitable formulation for successful LTG pharmacokinetic studies in rats.

IT 113170-86-8, Lamotrigine isethionate
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(influence of administration vehicles and drug formulations on pharmacokinetic profile of lamotrigine)

RN 113170-86-8 CAPLUS
CN Ethanesulfonic acid, 2-hydroxy-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (1:1) (9CI) (CA INDEX NAME)

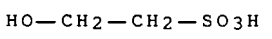
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

CRN 107-36-8
CMF C2 H6 O4 S



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 8 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:676002 CAPLUS Full-text
DOCUMENT NUMBER: 137:222039
TITLE: New crystal forms of lamotrigine and processes for their preparations
INVENTOR(S): Garti, Nissim; Berkovich, Yana; Dolitzky, Ben-Zion; Aronhime, Judith; Singer, Claude; Lieberman, Anita; Gershon, Neomi
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002068398	A1	20020906	WO 2002-US6160	20020227 <--
WO 2002068398	A9	20021121		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2439468	A1	20020906	CA 2002-2439468	20020227 <--
AU 2002240556	A1	20020912	AU 2002-240556	20020227 <--
US 2003018030	A1	20030123	US 2002-86157	20020227 <--
US 6861426	B2	20050301		
EP 1390355	A2	20040225	EP 2002-706471	20020227 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004526714	T	20040902	JP 2002-567912	20020227 <--
US 2005171107	A1	20050804	US 2005-45355	20050131 <--

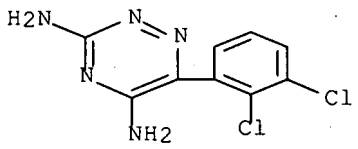
PRIORITY APPLN. INFO.:
US 2001-271688P P 20010227 <--
US 2002-86157 A1 20020227 <--
WO 2002-US6160 W 20020227 <--

AB The present invention relates to lamotrigine, a useful agent for anti-epilepsia. New crystal forms of lamotrigine-containing mols. of the solvent in stoichiometric ratios are disclosed. Processes for preparing the new crystal forms of lamotrigine and dosage forms are also provided. For example, 2 g of lamotrigine anhydrous and about 80 mL of ethanol were charged in a three-necked bottomed round flask equipped with a mech. stirrer, a condenser

and a thermometer. The suspension was stirred for about 24 h without heating at about 25° and the solid phase was separated by filtration, producing lamotrigine Form H, i.e., lamotrigine ethanol monosolvate.

IT 375347-20-9, Lamotrigine hydrate 454695-00-2
RL: CPS (Chemical process); FMU (Formation, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process); USES (Uses)
(preparation of crystal forms of lamotrigine as antiepileptic)

RN 375347-20-9 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)-, monohydrate (9CI) (CA INDEX NAME)

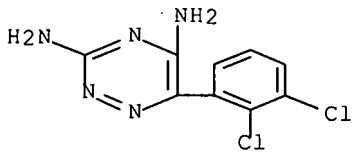


● H2O

RN 454695-00-2 CAPLUS
CN 2-Propanone, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (9CI) (CA INDEX NAME)

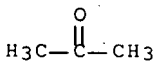
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

CRN 67-64-1
CMF C3 H6 O



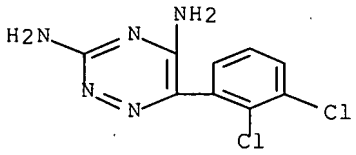
IT 454695-02-4 454695-03-5 454695-04-6

454695-05-7 454695-06-8 454695-07-9
454695-08-0 454695-09-1 454695-10-4
454695-11-5 454695-12-6 454695-13-7
454695-15-9
RL: FMU (Formation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(preparation of crystal forms of lamotrigine as antiepileptic)

RN 454695-02-4 CAPLUS
CN Formamide, N,N-dimethyl-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (1:1) (9CI) (CA INDEX NAME)

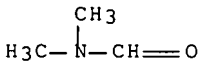
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

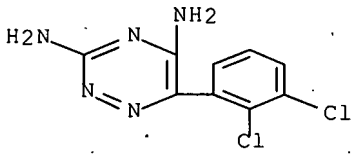
CRN 68-12-2
CMF C3 H7 N O



RN 454695-03-5 CAPLUS
CN 2-Propanol, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (9CI) (CA INDEX NAME)

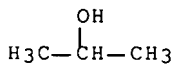
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

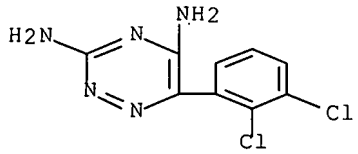
CRN 67-63-0
CMF C3 H8 O



RN 454695-04-6 CAPLUS
CN Formamide, N,N-dimethyl-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (3:2) (CA INDEX NAME)

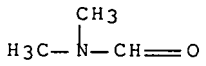
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

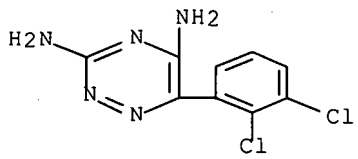
CRN 68-12-2
CMF C3 H7 N O



RN 454695-05-7 CAPLUS
CN Formamide, N,N-dimethyl-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (2:3) (9CI) (CA INDEX NAME)

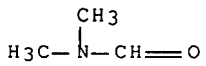
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

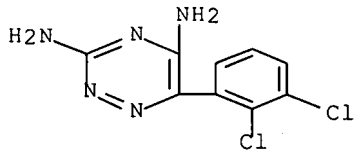
CRN 68-12-2
CMF C3 H7 N O



RN 454695-06-8 CAPLUS
CN Methanol, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (2:3) (9CI) (CA INDEX NAME)

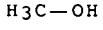
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

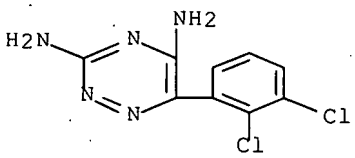
CRN 67-56-1
CMF C H4 O



RN 454695-07-9 CAPLUS
CN Ethanol, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (2:3) (9CI) (CA INDEX NAME)

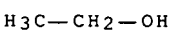
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

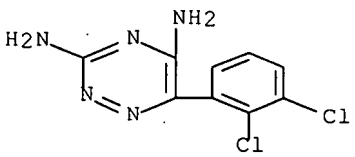
CRN 64-17-5
CMF C2 H6 O



RN 454695-08-0 CAPLUS
CN 2-Propanone, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (1:3) (9CI) (CA INDEX NAME)

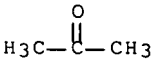
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

CRN 67-64-1
CMF C3 H6 O

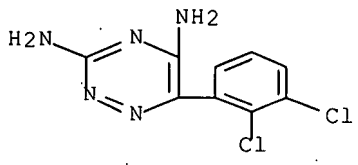


RN 454695-09-1 CAPLUS
CN Ethanol, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine

(1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

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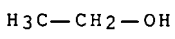
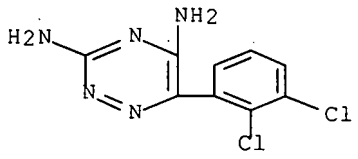
CMF C2 H6 O



RN 454695-10-4 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)-, compd. with tetrahydrofuran (9CI) (CA INDEX NAME)

CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



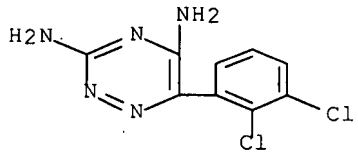
CM 2

CRN 109-99-9
CMF C4 H8 O

RN 454695-11-5 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)-, compd. with N-methylmethanamine (9CI) (CA INDEX NAME)

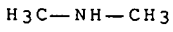
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

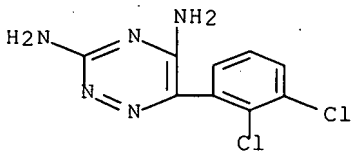
CRN 124-40-3
CMF C2 H7 N



RN 454695-12-6 CAPLUS
CN 2-Propanol, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (1:1) (9CI) (CA INDEX NAME)

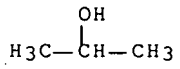
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

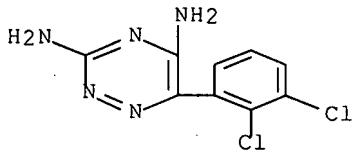
CRN 67-63-0
CMF C3 H8 O



RN 454695-13-7 CAPLUS
CN 2-Pentanone, 4-methyl-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (1:1) (9CI) (CA INDEX NAME)

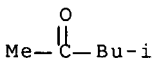
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

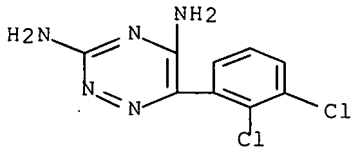
CRN 108-10-1
CMF C6 H12 O



RN 454695-15-9 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)-, compd. with 2-methoxy-2-methylpropane (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



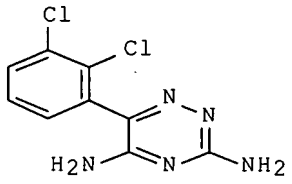
CM 2

CRN 1634-04-4
CMF C5 H12 O

t-Bu—O—Me

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 9 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:549382 CAPLUS Full-text
DOCUMENT NUMBER: 138:24695
TITLE: Synthesis of stable isotopically labelled versions of Lamotrigine and its methylated metabolite
AUTHOR(S): Manning, Calvin O.; Wadsworth, Alan H.; Fellows, Ian
CORPORATE SOURCE: Chemical Development, GlaxoSmithKline Research and Development, Stevenage, SG1 2NY, UK
SOURCE: Journal of Labelled Compounds & Radiopharmaceuticals (2002), 45(7), 611-618
CODEN: JLCRD4; ISSN: 0362-4803
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:24695
GI



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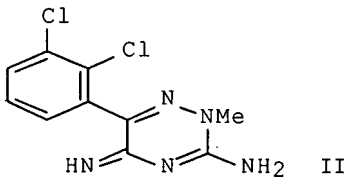
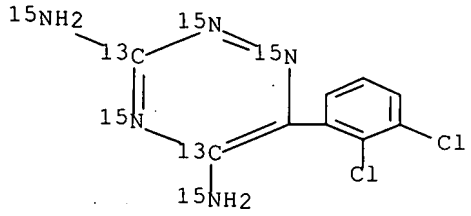


II

AB Lamotrigine (I) is a sodium channel antagonist used for the treatment of epilepsy. Stable isotopically labeled [M + 7] analogs of I and of its N-methylated metabolite II were prepared using [M + 5] labeled [13C, 15N4]-aminoguanidine, obtained from labeled thiourea. The overall yield for isotopically labeled II was 34% from [M + 3] labeled [13C, 15N2]-thiourea.

IT 478189-71-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of isotopically labeled (dichlorophenyl)diaminotriazine and (dichlorophenyl)methyl(amino)iminotriazine as analogs of Lamotrigine and its methylated metabolite)

RN 478189-71-8 CAPLUS
CN 1,2,4-Triazine-3,5-diamine-3,5-13C2-N,N',1,2,4-15N5, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



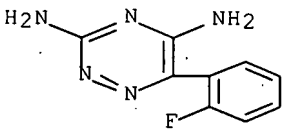
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 10 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:442736 CAPLUS Full-text
DOCUMENT NUMBER: 137:216626
TITLE: Infrared and Raman spectra of 3,5-diamino-6-(o-C6H4X)-1,2,4-triazines [X=F, Cl, Br, CH3]
AUTHOR(S): Withnall, Robert; Chowdhry, Babur Z.
CORPORATE SOURCE: School of Chemical and Life Sciences, University of Greenwich, London, SE18 6PF, UK
SOURCE: Spectrochimica Acta, Part A: Molecular and Biomolecular Spectroscopy (2002), 58A(8), 1721-1729
CODEN: SAMCAS; ISSN: 1386-1425
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

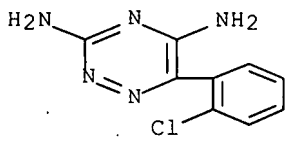
AB Raman and IR spectra of four substituted 3,5-diamino-6-(ortho-substituted phenyl)-1,2,4-triazines, having ortho-fluoro, -chloro, -bromo and -Me groups on the Ph ring, are reported and discussed. Bands due to substituent sensitive Ph vibrations are observed in both the Raman and IR spectra. The Raman spectra of all four compds. have strong bands near 770 and 1330 cm-1 which are assigned to the ring breathing vibration of the 1,2,4-triazine ring and an asym. triazine C-NH2 stretching vibration, resp. A medium/strong band near 800 cm-1 in the IR spectra is attributed to an out-of-plane bending vibration of the substituted 1,2,4-triazine ring.

IT 35857-42-2 38943-73-6 77668-49-6
RL: PRP (Properties)
(IR and Raman spectra of 3,5-diamino-6-(o-C6H4X)-1,2,4-triazines [X=F, Cl, Br, CH3])

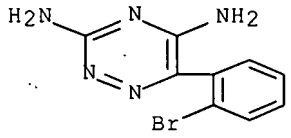
RN 35857-42-2 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



RN 38943-73-6 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2-chlorophenyl)- (9CI) (CA INDEX NAME)



RN 77668-49-6 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2-bromophenyl)- (9CI) (CA INDEX NAME)

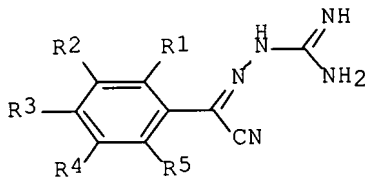


REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

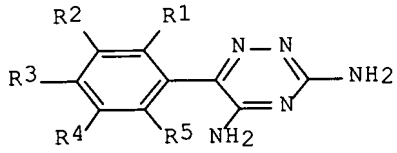
L21 ANSWER 11 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:631908 CAPLUS Full-text
DOCUMENT NUMBER: 135:195578
TITLE: Process for preparing substituted benzoyl cyanide amidinohydrazones as intermediates for synthesis of 3,5-diamino-6-phenyl-1,2,4-triazines
INVENTOR(S): Nadaka, Vladimir; Lexner, Jael; Kaspi, Joseph
PATENT ASSIGNEE(S): Chemagis Ltd., Israel
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1127873	A2	20010829	EP 2001-103660	20010223 <--
EP 1127873	A3	20030507		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
IL 134730	A	20031031	IL 2000-134730	20000225 <--
CA 2337280	A1	20010825	CA 2001-2337280	20010215 <--
HU 200100740	A2	20011128	HU 2001-740	20010215 <--
US 2001025118	A1	20010927	US 2001-789634	20010222 <--
US 6329521	B2	20011211		

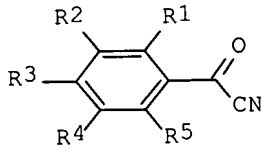
PRIORITY APPLN. INFO.: IL 2000-134730 A 20000225 <--
OTHER SOURCE(S): CASREACT 135:195578; MARPAT 135:195578
GI



I



II

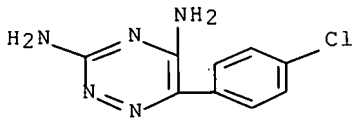


III

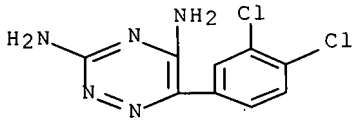
AB The title compds. [I; R1-R5 = H, halo, alkyl, etc.], useful as intermediates for synthesis of 1,2,4-triazines II (active in the treatment of CNS disorders), were prepared by reacting the benzoyl cyanides III with aminoguanidine bicarbonate in a mixture of a water-soluble solvent and polyphosphoric acid. Thus, reacting 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in the presence of polyphosphoric acid in MeCN afforded 2,3-dichlorobenzoyl cyanide amidinohydrazone which was then heated under reflux in PrOH to give 2,3-diamino-6-(2,3-dichlorophenyl)- 1,2,4-triazine.

IT 6662-28-8P 36518-85-1P 38943-76-9P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for preparing substituted benzoyl cyanide amidinohydrazones as intermediates for synthesis of 3,5-diamino-6-phenyl-1,2,4-triazines)

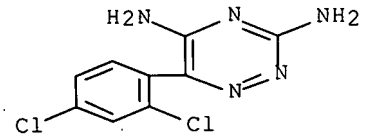
RN 6662-28-8 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(4-chlorophenyl)- (9CI) (CA INDEX NAME)



RN 36518-85-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(3,4-dichlorophenyl)- (9CI) (CA INDEX NAME)



RN 38943-76-9 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,4-dichlorophenyl)- (9CI) (CA INDEX NAME)

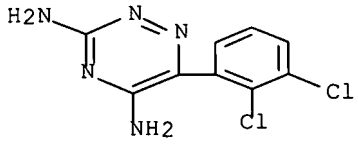


L21 ANSWER 12 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:499101 CAPLUS Full-text
DOCUMENT NUMBER: 136:5580
TITLE: Hydrogen bonding patterns in 3,5-diamino-6-aryl triazines
AUTHOR(S): Kubicki, M.; Codding, P. W.
CORPORATE SOURCE: Faculty of Chemistry, Laboratory of Crystallography, Adam Mickiewicz University, Poznan, 60-780, Pol.
SOURCE: Journal of Molecular Structure (2001), 570(1-3), 53-60
CODEN: JMOSB4; ISSN: 0022-2860
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The crystal structure of two related 1,2,4-triazine derivs., C9H7N5Cl2·H2O (I) and C12H14N5Cl2+·CH3SO3-·H2O (II) that have different biol. effects, have been determined Lamotrigine (Lamictal), I, is a novel anticonvulsant and BWA256C, II, is a class 1 antiarrythmic drug. The dihedral angles between the least-squares planes of almost exactly planar Ph and triazine rings are 76.42(6) and 76.08(6)°, for compds. I and II, resp. In II, protonation takes place at the iminium nitrogen atom, thus suggesting the importance of resonance through the triazine ring. This resonance is also confirmed by the pattern of bond lengths and angles. Extensive networks of hydrogen bonds, in which all mol. species are involved, rule the crystal packing in both compds. The anal. of hydrogen bond networks in other 3,5-diamino-6-aryl derivs. suggests that there is a strong influence of co-crystallizing solvent mol. on the nature of resulting hydrogen bond topol.

IT 375347-20-9, Lamotrigine hydrate
RL: PRP (Properties)
(crystal structure; hydrogen bonding patterns in crystal structure of 3,5-diamino-6-aryl triazines)

RN 375347-20-9 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)-, monohydrate (9CI) (CA INDEX NAME)



● H2O

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 13 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:369058 CAPLUS Full-text
DOCUMENT NUMBER: 136:14957
TITLE: Isolation of lamotrigine 2-N-glucuronide from guinea pig urine
AUTHOR(S): Yeh, Shih-Woei; Yu, Hsiu-Ying
CORPORATE SOURCE: School of Pharmacy, National Taiwan University, Taipei, 100, Taiwan
SOURCE: Chinese Pharmaceutical Journal (Taipei, Taiwan) (2000), 52(5), 241-249
CODEN: CPHJEP; ISSN: 1016-1015
PUBLISHER: Pharmaceutical Society of Republic of China
DOCUMENT TYPE: Journal
LANGUAGE: English

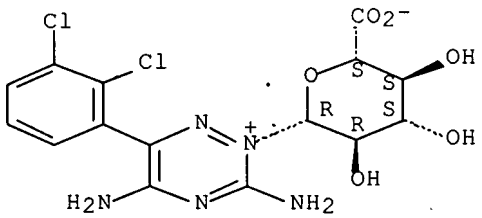
AB Lamotrigine (LT) is a novel anticonvulsant. Its major metabolite in human is 2-N-glucuronide (LT-2NG). In order to investigate the metabolic characteristics of LT in our laboratory, a reference standard of LT-2NG was required. The purpose of this experiment was to isolate pure LT-2NG from the urine of LT-treated guinea pigs. The pooled urine of guinea pigs fed with LT was eluted with methanol through XAD-2 column. LT-2NG in the eluent was purified by semi-preparative HPLC equipped with a C8 column and a UV detector set at 267 nm. The mobile phase for HPLC was 0.01M ammonium acetate (pH 6.6) containing 12% of methanol. The isolated LT-2NG was confirmed by mass, 1H NMR and 13C NMR spectroscopic anal. The mol. ion 432.1, a downfield anomeric proton at 5.39 ppm, and an upfield shift (-6.9 ppm) of the triazine ring C-3 indicate attachment of the glucuronide to the N-2 of LT. These spectra were identical with the reported spectra of LT-2NG isolated from human urine.

IT 135288-68-5P
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); ANST (Analytical study); BIOL (Biological study); PREP (Preparation)
(isolation of lamotrigine 2-N-glucuronide from guinea pig urine)

RN 135288-68-5 CAPLUS

CN 1,2,4-Triazinium, 3,5-diamino-6-(2,3-dichlorophenyl)-2-β-D-glucopyranuronosyl-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 14 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:240093 CAPLUS Full-text
DOCUMENT NUMBER: 132:301224

TITLE: 3,5-Diamino-6-(2-fluorophenyl)-1,2,4-triazine-dimethylformamide (1/1)

AUTHOR(S): Janes, Robert W.
CORPORATE SOURCE: School of Biological Sciences, Queen Mary and Westfield College, University of London, London, E1 4NS, UK

SOURCE: Acta Crystallographica, Section C: Crystal Structure Communications (2000), C56(3), 362-364
CODEN: ACSCEE; ISSN: 0108-2701
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The title compound, C9H8FN5·C3H7NO, contains two independent complexes in the asym. unit, each consisting of one 3,5-diamino-6-(2- fluorophenyl)-1,2,4-triazine mol. and one DMF solvent mol. One triazine mol. is disordered over two conformations within the crystal, the occupancies being 62(1) and 38(1)%. The Ph ring of this mol. resolves into two conformations rotated by almost 180° about the bridging bond between the two rings, while the triazine rings approx. superimpose on each other. The triazine mols. of the asym. unit differ in the dihedral angles between their resp. Ph and triazine ring planes, these being 57.6(2)° for the fully occupied, and 76.9(6) and 106.8(8)° for the partially occupied mols. An extensive network of H bonds maintains the crystal structure. Crystallog. data are given.

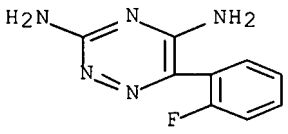
IT 264616-05-9, 3,5-Diamino-6-(2-fluorophenyl)-1,2,4-triazine compound with dimethylformamide (1:1)
RL: PRP (Properties)
(crystal structure of)

RN 264616-05-9 CAPLUS

CN Formamide, N,N-dimethyl-, compd. with 6-(2-fluorophenyl)-1,2,4-triazine-3,5-diamine (1:1) (9CI) (CA INDEX NAME)

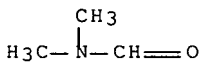
CM 1

CRN 35857-42-2
CMF C9 H8 F N5



CM 2

CRN 68-12-2
CMF C3 H7 N O



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 15 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:56846 CAPLUS Full-text
DOCUMENT NUMBER: 132:303346
TITLE: Effects of co-administration of anticonvulsant and putative anticonvulsive agents and sub-/suprathreshold doses of L-Dopa upon motor behaviour of MPTP-treated mice
AUTHOR(S): Fredriksson, A.; Palomo, T.; Archer, T.
CORPORATE SOURCE: Department of Psychiatry, Ullerakers Hospital, University of Uppsala, Uppsala, Swed.
SOURCE: Journal of Neural Transmission (1999), 106(9-10), 889-909
CODEN: JNTRF3; ISSN: 1435-1463
PUBLISHER: Springer-Verlag Wien
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of co-administration of the dopamine precursor, L-Dopa, with anticonvulsant and putative anticonvulsive agents upon the motor activity of hypoactive MPTP-treated C57 BL/6 mice were measured in six expts. In each case, MPTP (2+40 mg/kg, s.c., separated by a 24-h interval) was administered four to six weeks prior to behavioral testing. Thus, the effects of these agents combined with either a single acute, subthreshold dose (5 mg/kg, s.c.) of L-Dopa, or, with chronically-administered, suprathreshold doses (20 mg/kg, s.c.) of L-Dopa were studied. In the former, lamotrigine, FCE 26743 and L-Deprenyl, injected 60 min before subthreshold L-Dopa (5 mg/kg), each induced an antiparkinsonian action in MPTP-treated mice that consisted of dose-specific, as opposed to dose-related, elevations of locomotion and rearing behavior. In the latter, lamotrigine (all three measures of activity at 3 mg/kg), FCE 26743 (locomotion and total activity at 3; rearing at 1 and 3 mg/kg) and L-Deprenyl (locomotion and total activity at 1 and 3 mg/kg), but not phenytoin (neither at 1 nor 3 mg/kg), reinstated the motor activity-stimulating effects of the threshold dose of L-Dopa (20 mg/kg) in L-Dopa-tolerant, MPTP-treated mice. Neurochem. analyses confirmed severe DA depletions in MPTP-treated mice. Since neither lamotrigine, FCE 26743 nor L-Deprenyl, nor subthreshold L-Dopa, by themselves increased the motor behavior of MPTP-treated mice, a synergistic effect of the co-administration is concluded. Further, since the suprathreshold dose of L-Dopa by itself failed to stimulate motor activity in the MPTP mice following chronic (25 daily injections) administrations of the compound, it is suggested that a restorative effect, in combination with lamotrigine, FCE 26743 or L-Deprenyl was evidenced. The potential therapeutic benefits of anticonvulsant or putative anticonvulsive compds. for parkinsonian symptoms are discussed.

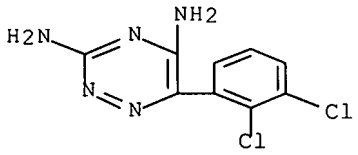
IT 113170-86-8, Lamotrigine isethionate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of co-administration of anticonvulsant and putative anticonvulsive agents and sub-/suprathreshold doses of L-Dopa upon motor behavior of MPTP-treated mice in relation to antiparkinsonian effects)

RN 113170-86-8 CAPLUS
CN Ethanesulfonic acid, 2-hydroxy-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (1:1) (9CI) (CA INDEX NAME)

CM 1

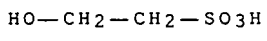
CRN 84057-84-1

CMF C9 H7 Cl2 N5



CM 2

CRN 107-36-8
CMF C2 H6 O4 S



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 16 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:12098 CAPLUS Full-text
DOCUMENT NUMBER: 132:130210
TITLE: Structure of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine isethionate solvate (lamotrigine isethionate)
AUTHOR(S): Potter, Brian; Palmer, Rex A.; Withnall, Robert; Leach, Michael J.; Chowdhry, Babur Z.
CORPORATE SOURCE: Department of Crystallography, Birkbeck College, University of London, London, WC1E 7HX, UK
SOURCE: Journal of Chemical Crystallography (1999), 29(6), 701-706
CODEN: JCCYEV; ISSN: 1074-1542
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

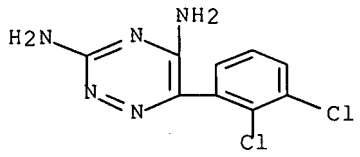
AB The crystal and mol. structure of lamotrigine isethionate was determined by direct methods. The compound crystallizes in the tetragonal space group I41/a, with a 19.684(5), c 16.557(5) Å; Z = 16, dc = 1.579; R = 0.0532, Rw = 0.1317 for 2041 reflections. Atomic coordinates are given. The isethionate moiety forms multiple H bonds to the lamotrigine nucleus, three from one isethionate, two from a symmetry related isethionate and a further two from two different symmetry related mols. Protonation of N(2') in the triazine ring, not observed in the native lamotrigine structure is presumably associated with the interaction of the isethionate moiety. Both rings in the lamotrigine moiety are essentially planar, with a dihedral angle of 66.08(7)° compared to 80.70° in native lamotrigine. The connecting bond length C(1)-C(6') 1.493(3) Å also correlates well with values in related compds. (1.480(3) Å) in the native structures.

IT 113170-86-8, Lamotrigine isethionate
RL: PRP (Properties)
(crystal structure of)
RN 113170-86-8 CAPLUS

CN Ethanesulfonic acid, 2-hydroxy-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (1:1) (9CI) (CA INDEX NAME)

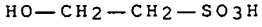
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

CRN 107-36-8
CMF C2 H6 O4 S



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 17 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:795469 CAPLUS Full-text
DOCUMENT NUMBER: 132:26963
TITLE: Preparation of 1,2,4-triazine derivative, and its use as reference marker for testing purity and stability of lamotrigine
INVENTOR(S): Edmeades, Lorraine Mary; Griffith-Skinner, Nigel Arthur; Hill, Derek Anthony; Hill, Graham Thornton; Packham, Terrence William
PATENT ASSIGNEE(S): The Wellcome Foundation Limited, UK
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 963980	A2	19991215	EP 1999-200695	19990310 <--
EP 963980	A3	20000531		
EP 963980	B1	20020605		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
SG 85628	A1	20020115	SG 1999-1252	19990225 <--
MX 9902202	A	20000831	MX 1999-2202	19990305 <--

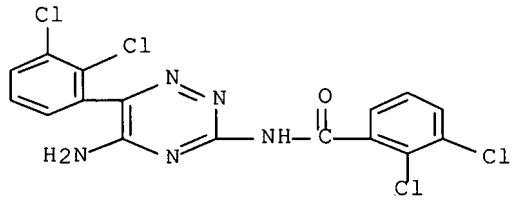
KR 2000005611	A	20000125	KR 1999-7632	19990309	<--
HR 990074	A1	20001031	HR 1999-74	19990309	<--
ZA 9901951	A	19990816	ZA 1999-1951	19990310	<--
JP 2989189	B2	19991213	JP 1999-63792	19990310	<--
JP 2000009714	A	20000114			
NO 9901151	A	19991213	NO 1999-1151	19990310	<--
CN 1238454	A	19991215	CN 1999-103445	19990310	<--
AU 9920319	A	20000106	AU 1999-20319	19990310	<--
TR 9900520	A2	20000121	TR 1999-520	19990310	<--
HU 9900592	A2	20000428	HU 1999-592	19990310	<--
BR 9900984	A	20000502	BR 1999-984	19990310	<--
NZ 334590	A	20000728	NZ 1999-334590	19990310	<--
CA 2265194	C	20001010	CA 1999-2265194	19990310	<--
US 6333198	B1	20011225	US 1999-265670	19990310	<--
EP 1170588	A1	20020109	EP 2001-203376	19990310	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
AT 218552	T	20020615	AT 1999-200695	19990310	<--
PT 963980	T	20021031	PT 1999-200695	19990310	<--
ES 2178342	T3	20021216	ES 1999-200695	19990310	<--
CN 1306210	A	20010801	CN 2000-122208	20000725	<--
US 2002055177	A1	20020509	US 2001-940422	20010829	<--
NO 2003002753	A	19991213	NO 2003-2753	20030617	<--
PRIORITY APPLN. INFO.:			GB 1998-12413	A 19980610	<--
			EP 1999-200695	A3 19990310	<--
			US 1999-265670	A3 19990310	<--

AB A method of testing the purity or stability to degradation of a sample of lamotrigine or a pharmaceutical dosage form comprising lamotrigine consists of assaying the sample for the presence of a compound selected from 3-amino-6-(2,3-dichlorophenyl)-1,2,4-triazine-5-(4H)-one and N-[5-amino-6-(2,3-dichlorophenyl)-1,2,4-triazine-3-yl]-2,3- dichlorobenzamide (I). A process for producing compound I, is also disclosed. Lamotrigine was treated with 2,3-dichlorobenzoyl chloride to give I. TLC-densitometry was used to determine I in lamotrigine tablets.

IT 252186-79-1P
RL: ANT (Analyte); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation)
(preparation of triazine derivative as reference marker for testing purity and
stability of lamotrigine)

RN 252186-79-1 CAPLUS

CN Benzamide, N-[5-amino-6-(2,3-dichlorophenyl)-1,2,4-triazin-3-yl]-2,3-dichloro- (9CI) (CA INDEX NAME)



L21 ANSWER 18 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:466614 CAPLUS Full-text

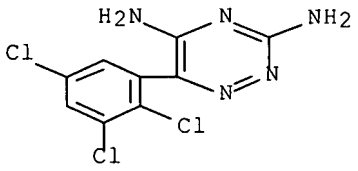
DOCUMENT NUMBER: 131:192059
TITLE: Crystal structure of an analog of the anticonvulsant lamotrigine, 3,5-diamino-6-(2,3,5-trichlorophenyl)-1,2,4-triazine·dimethanolate, and structure comparisons with related analogs
AUTHOR(S): Janes, Robert W.
CORPORATE SOURCE: School of Biological Sciences, Queen Mary and Westfield College, University of London, London, E1 4NS, UK
SOURCE: Journal of Chemical Crystallography (1999), 29(2), 163-167
CODEN: JCCYEV; ISSN: 1074-1542
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 3,5-Diamino-6-(2,3,5-trichlorophenyl)-1,2,4-triazine crystallizes with two MeOH solvent mols. in the triclinic space group P.hivin.1, with a 7.372(4), b 10.476(4), c 11.863(11) Å, α 72.18(5), β 79.73(6), γ 79.47(4)°; dc = 1.385, Z = 2; R1 = 0.0405, Rw2 = 0.1156 for 2437 reflections. Atomic coordinates are given. There is substantial distortion between the Ph and triazine rings as illustrated by the value of the nonbonded angle C3t-C6t-C4 of 173.60° and the C4 atom being -0.4487 Å from the plane calculated for the triazine ring atoms. The lengths of the bonds of the triazine moiety suggest that there is a potential decrease in the degree of aromaticity of the ring. Comparisons are made between this structure, and other lamotrigine analog structures that are reported.

IT 240125-64-8, 3,5-Diamino-6-(2,3,5-trichlorophenyl)-1,2,4-triazine compound with methanol (1:2)
RL: PRP (Properties)
(crystal structure of)
RN 240125-64-8 CAPLUS
CN Methanol, compd. with 6-(2,3,5-trichlorophenyl)-1,2,4-triazine-3,5-diamine (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 77668-56-5
CMF C9 H6 Cl3 N5



CM 2

CRN 67-56-1
CMF C H4 O

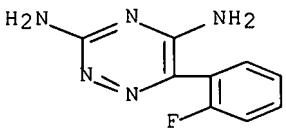
H3C—OH

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 19 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:7243 CAPLUS Full-text
DOCUMENT NUMBER: 130:191428
TITLE: The antiepileptic lamotrigine and its analogs: comparative theoretical electronic properties
AUTHOR(S): De Oliveira Neto, Marcal; Pires, Jose M.; Giambiagi, Mario; De Giambiagi, Myriam Segre; Alvarez, Fernando A.
CORPORATE SOURCE: Departmento de Quimica, Universidade de Brasilia, Campus Universitario Asa Norte, Brasilia D. F., 70910-900, Brazil
SOURCE: Structural Chemistry (1998), 9(5), 339-348
CODEN: STCHES; ISSN: 1040-0400
PUBLISHER: Plenum Publishing Corp.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Electronic properties of lamotrigine (LTG) and two analogs (A1 and A2) are compared through MOPAC-AM1 calcns. Two stable conformers of LTG are calculated to exist in agreement with X-ray crystallog. In the three compds. and the two conformers for each of them, the more favorable protonation sites are N2 and N4; these should then be the sites appropriate for interaction with a receptor, and group valence reinforces the supposition. The mol. electrostatic potentials show that a region between the two chlorine atoms in LTG could be the site for an electrostatic interaction with a corresponding site in the receptor. The fluorine atom in A1 would play an equivalent role. A simple model for LTG-receptor interaction is proposed.

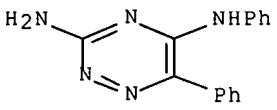
IT 35857-42-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiepileptic lamotrigine and its analogs: comparative theor. electronic properties and receptor interaction modeling)
RN 35857-42-2 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



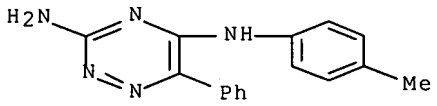
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 20 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:267055 CAPLUS Full-text
DOCUMENT NUMBER: 129:4628
TITLE: Study on the syntheses of new 1-(o-chlorobenzoyl)-3-(5'-substituted phenylamino-6'-phenyl)-1',2',4'-triazinylureas

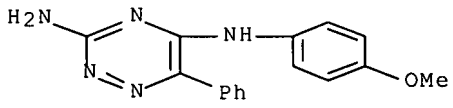
AUTHOR(S): Zou, Jian-Ping; Zeng, Run-Sheng; Wang, Ai-Fen; Lu, Zhong-E.
CORPORATE SOURCE: Department of Chemistry, Suzhou University, Suzhou, 215006, Peop. Rep. China
SOURCE: Chinese Journal of Chemistry (1998), 16(1), 58-64
CODEN: CJOCEV; ISSN: 1001-604X
PUBLISHER: Science Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Eight new 1-(o-chlorobenzoyl)-3-(5'-substituted phenylamino-6'-phenyl)-1',2',4'-triazinylureas have been synthesized and their bioactivities were detected.
IT 142706-34-1P 146330-32-7P 146330-33-8P
146330-35-0P 146330-36-1P 207460-72-8P
207460-73-9P 207460-74-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of chlorobenzoyl-substituted triazinylureas)
RN 142706-34-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, N5,6-diphenyl- (9CI) (CA INDEX NAME)



RN 146330-32-7 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, N5-(4-methylphenyl)-6-phenyl- (9CI) (CA INDEX NAME)

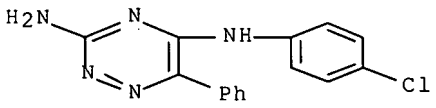


RN 146330-33-8 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, N5-(4-methoxyphenyl)-6-phenyl- (9CI) (CA INDEX NAME)

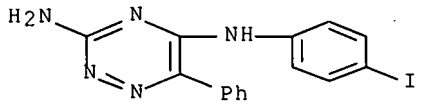


RN 146330-35-0 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, N5-(4-chlorophenyl)-6-phenyl- (9CI) (CA INDEX

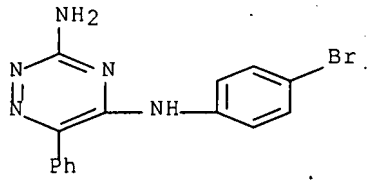
NAME)



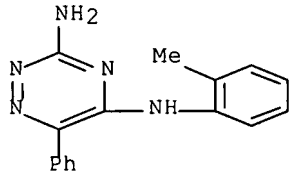
RN 146330-36-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, N5-(4-iodophenyl)-6-phenyl- (9CI) (CA INDEX NAME)



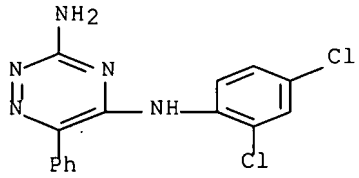
RN 207460-72-8 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, N5-(4-bromophenyl)-6-phenyl- (9CI) (CA INDEX NAME)



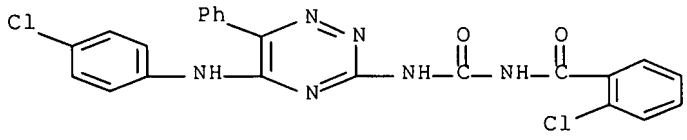
RN 207460-73-9 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, N5-(2-methylphenyl)-6-phenyl- (9CI) (CA INDEX NAME)



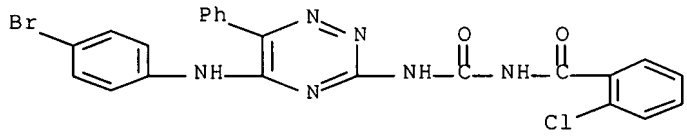
RN 207460-74-0 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, N5-(2,4-dichlorophenyl)-6-phenyl- (9CI) (CA INDEX NAME)



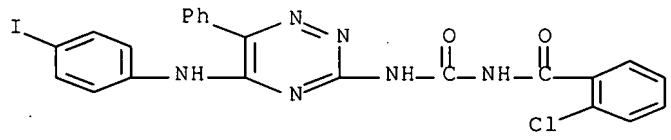
IT 207460-75-1P 207460-76-2P 207460-77-3P
207460-78-4P 207460-80-8P 207460-82-0P
207460-84-2P 207460-86-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of chlorobenzoyl-substituted triazinylureas)
RN 207460-75-1 CAPLUS
CN Benzamide, 2-chloro-N-[[[5-[(4-chlorophenyl)amino]-6-phenyl-1,2,4-triazin-3-yl]amino]carbonyl]- (9CI) (CA INDEX NAME)



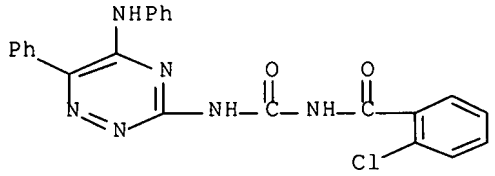
RN 207460-76-2 CAPLUS
CN Benzamide, N-[[[5-[(4-bromophenyl)amino]-6-phenyl-1,2,4-triazin-3-yl]amino]carbonyl]-2-chloro- (9CI) (CA INDEX NAME)



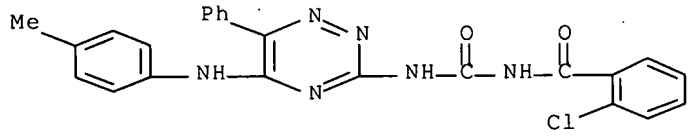
RN 207460-77-3 CAPLUS
CN Benzamide, 2-chloro-N-[[[5-[(4-iodophenyl)amino]-6-phenyl-1,2,4-triazin-3-yl]amino]carbonyl]- (9CI) (CA INDEX NAME)



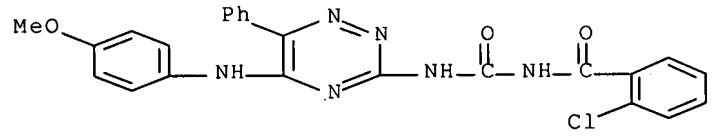
RN 207460-78-4 CAPLUS
CN Benzamide, 2-chloro-N-[[[6-phenyl-5-(phenylamino)-1,2,4-triazin-3-yl]amino]carbonyl]- (9CI) (CA INDEX NAME)



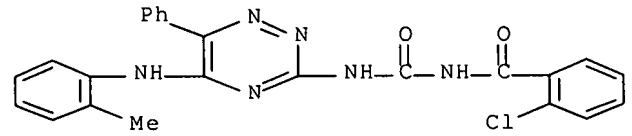
RN 207460-80-8 CAPLUS
CN Benzamide, 2-chloro-N-[[[5-[(4-methylphenyl)amino]-6-phenyl-1,2,4-triazin-3-yl]amino]carbonyl]- (9CI) (CA INDEX NAME)



RN 207460-82-0 CAPLUS
CN Benzamide, 2-chloro-N-[[[5-[(4-methoxyphenyl)amino]-6-phenyl-1,2,4-triazin-3-yl]amino]carbonyl]- (9CI) (CA INDEX NAME)

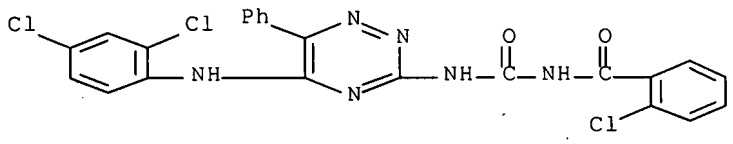


RN 207460-84-2 CAPLUS
CN Benzamide, 2-chloro-N-[[[5-[(2-methylphenyl)amino]-6-phenyl-1,2,4-triazin-3-yl]amino]carbonyl]- (9CI) (CA INDEX NAME)



RN 207460-86-4 CAPLUS

CN Benzamide, 2-chloro-N-[[[5-[(2,4-dichlorophenyl)amino]-6-phenyl-1,2,4-triazin-3-yl]amino]carbonyl]- (9CI) (CA INDEX NAME)



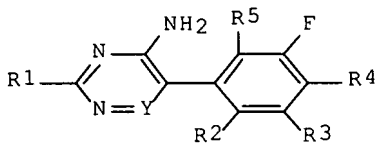
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 21 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:473716 CAPLUS Full-text
DOCUMENT NUMBER: 127:81468
TITLE: Fluorophenyl-triazine and pyrimidine derivatives as compounds acting on the central nervous system
INVENTOR(S): Torrens Jover, Antoni; Frigola Constansa, Jordi
PATENT ASSIGNEE(S): Laboratorios Del Dr. Esteve, S.A., Spain; Torrens Jover, Antoni; Frigola Constansa, Jordi
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

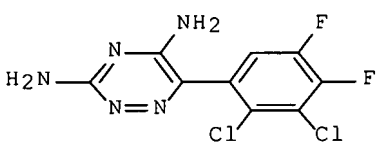
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9720827	A1	19970612	WO 1996-EP5593	19961204 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2741879	A1	19970606	FR 1995-14354	19951205 <--
AU 9711943	A	19970627	AU 1997-11943	19961204 <--
ES 2128960	A1	19990516	ES 1996-2667	19961205 <--
ES 2128960	B1	20000116		

PRIORITY APPLN. INFO.: FR 1995-14354 A 19951205 <--
WO 1996-EP5593 W 19961204 <--

OTHER SOURCE(S): CASREACT 127:81468; MARPAT 127:81468
GI



I

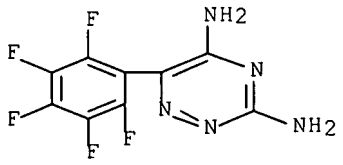


II

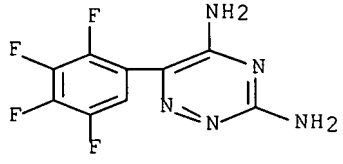
AB Novel fluorophenyl-triazine and pyrimidine derivs. I and their physiol. acceptable salts are disclosed [wherein R1 = amino, 1-piperazinyl or 4-alkylpiperazin-1-yl, where alkyl = C1-4 chain, preferably Me; R2, R3, R4 = halo, preferably F or Cl; R5 = H or halo, preferably F or Cl; Y = N, CH]. A method for preparing the compds. is also disclosed, as are pharmaceutical compns. containing a pharmaceutically acceptable carrier and at least one such compound The compds. are CNS agents which act by inhibiting the release of glutamate. Examples include 13 syntheses, 1 standard formulation, and biol. data for 5 compds. For instance, 2,3-dichloro-4,5-difluorobenzoic acid (prepared in 3 steps) was converted to the acid chloride (99%) and then to the acyl cyanide (98%), and the latter was condensed with aminoguanidine bicarbonate and cyclized (31%) to give title compound II. In a test for prevention of hypoxic death in mice, II had an ED50 of 0.6 mg/kg i.p., vs. 1.2 mg/kg for lamotrigine.

IT 191872-71-6P, 3,5-Diamino-6-(2,3,4,5,6-pentafluorophenyl)-1,2,4-triazine 191872-72-7P, 3,5-Diamino-6-(2,3,4,5-tetrafluorophenyl)-1,2,4-triazine 191872-73-8P, 3,5-Diamino-6-(2,3,5,6-tetrafluorophenyl)-1,2,4-triazine 191872-74-9P, 3,5-Diamino-6-(3-chloro-2,4,5-trifluorophenyl)-1,2,4-triazine 191872-75-0P, 3,5-Diamino-6-(2,3-dichloro-4,5-difluorophenyl)-1,2,4-triazine 191872-76-1P, 3,5-Diamino-6-(2,3,4-trichloro-5-fluorophenyl)-1,2,4-triazine 191872-86-3P, 3,5-Diamino-6-(3,4-dichloro-2,5-difluorophenyl)-1,2,4-triazine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (fluorophenyl)triazine and -pyrimidine derivs. as CNS agents)

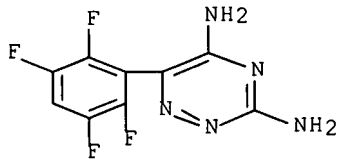
RN 191872-71-6 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(pentafluorophenyl)- (9CI) (CA INDEX NAME)



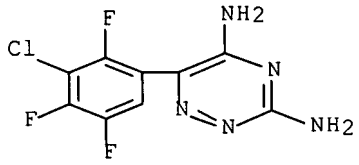
RN 191872-72-7 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3,4,5-tetrafluorophenyl)- (9CI) (CA INDEX NAME)



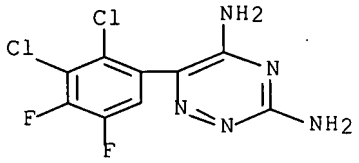
RN 191872-73-8 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3,5,6-tetrafluorophenyl)- (9CI) (CA INDEX NAME)



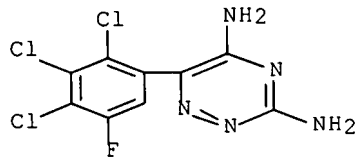
RN 191872-74-9 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(3-chloro-2,4,5-trifluorophenyl)- (9CI) (CA INDEX NAME)



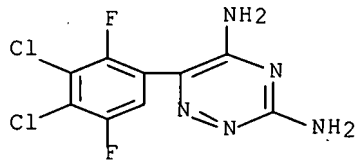
RN 191872-75-0 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichloro-4,5-difluorophenyl)- (9CI) (CA INDEX NAME)



RN 191872-76-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3,4-trichloro-5-fluorophenyl)- (9CI) (CA INDEX NAME)



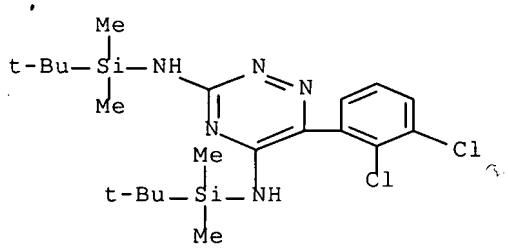
RN 191872-86-3 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(3,4-dichloro-2,5-difluorophenyl)- (9CI) (CA INDEX NAME)



L21 ANSWER 22 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:403479 CAPLUS Full-text
DOCUMENT NUMBER: 127:75452
TITLE: Lamotrigine analysis in plasma by gas chromatography-mass spectrometry after conversion to a tert-butyldimethylsilyl derivative
AUTHOR(S): Gasgupta, Amitava; Hart, Amy P.
CORPORATE SOURCE: Dep. Pathol., Univ. New Mexico Health Sci. Cent., Albuquerque, NM, 87106, USA
SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (1997), 693(1), 101-107
CODEN: JCBBEP; ISSN: 0378-4347
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A gas chromatog.-mass spectrometric method is described for the identification and quantitation of lamotrigine after extraction from human serum and derivatization. Lamotrigine was extracted from alkaline serum with CHCl3 and derivatized with N-methyl-N-(tert-butyldimethylsilyl)trifluoroac etamide containing 2% tert-butyldimethylchlorosilane. Oxazepam-d5 was used as an internal standard The tert-butyldimethylsilyl derivative of lamotrigine showed distinct mol. ions at m/z 483 and 485 as well as other peaks at m/z 426, 370 and 334 for unambiguous identification. The base peak was at m/z 199. Similarly, the tert-butyldimethylsilyl of oxazepam-d5 showed mol. ions at m/z 619 and 521, along with other characteristic peaks at m/z 462, 376 and 318. For the anal. of lamotrigine, the mass spectrometer was operated in the selective ion-monitoring mode. The within-run and between-run precisions were 4.3% and 5.1%, resp., at a serum lamotrigine concentration of 3.0 μg/mL. The within-run and between-run precisions were 8.2% and 10.6%, resp., at a serum lamotrigine concentration of 0.5 μg/mL. The assay was linear for serum lamotrigine concns. of 0.5=2.0 μg/mL. The detection limit was 0.25 μg/mL. The assay was free from interferences from common tricyclic antidepressants, benzodiazepines, other common anticonvulsants, salicylate and acetaminophen.

IT 191802-72-9P
RL: ANT (Analyte); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation)
(lamotrigine determination in human plasma after preparation of)
RN 191802-72-9 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)-N,N'-bis[(1,1-dimethylethyl)dimethylsilyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 23 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:172487 CAPLUS Full-text
DOCUMENT NUMBER: 126:176903
TITLE: Pharmaceutical composition containing lamotrigine
INVENTOR(S): Floyd, Alison Green; Jain, Sunil
PATENT ASSIGNEE(S): The Wellcome Foundation Limited, UK; Floyd, Alison Green; Jain, Sunil
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9700681	A1	19970109	WO 1996-EP2759	19960620 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
AU 9664157	A	19970122	AU 1996-64157	19960620 <--
EP 833640	A1	19980408	EP 1996-923914	19960620 <--
EP 833640	B1	20021204		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
JP 11507936	T	19990713	JP 1996-503591	19960620 <--
AT 228844	T	20021215	AT 1996-923914	19960620 <--
PT 833640	T	20030430	PT 1996-923914	19960620 <--
ES 2188766	T3	20030701	ES 1996-923914	19960620 <--
US 5942510	A	19990824	US 1997-973798	19971209 <--
PRIORITY APPLN. INFO.:			GB 1995-12854 A	19950623 <--
			WO 1996-EP2759 W	19960620 <--

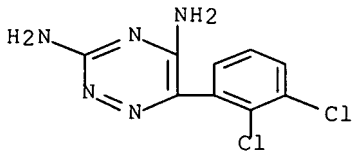
AB A lyophilized formulation of lamotrigine having been prepared by lyophilizing a frozen sterile aqueous solution of lamotrigine mesylate in which the pH is from 2.5 to 4. A freeze-dried pharmaceutical was prepared containing lamotrigine 25.0, mannitol 377.8, and methanesulfonic acid 93.75 mg/vial. The formulation was stable after storage for 6 mo ate 40° and 75% relative humidity and no loss in potency and no significant decomposition was observed

IT 187106-86-1, Lamotrigine mesylate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceutical composition containing lamotrigine)
RN 187106-86-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)-, monomethanesulfonate (9CI) (CA INDEX NAME)

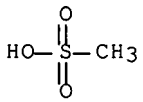
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

CRN 75-75-2
CMF C H4 O3 S



L21 ANSWER 24 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:145923 CAPLUS Full-text
DOCUMENT NUMBER: 126:194827
TITLE: Comparison of the pharmacokinetics of lamotrigine in patients with chronic renal failure and healthy volunteers
AUTHOR(S): Wootton, R.; Soul-Lawton, J.; Rolan, P. E.; Fook Sheung, C. T. C.; Cooper, J. D. H.; Posner, J.
CORPORATE SOURCE: Dept. of Clinical Pharm., Wellcome Res. Labs., Beckenham, UK
SOURCE: British Journal of Clinical Pharmacology (1997), 43(1), 23-27
CODEN: BCPHBM; ISSN: 0306-5251
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim of this study was to compare the pharmacokinetics of the antiepileptic agent, lamotrigine, in patients with chronic renal failure and healthy volunteers. Non-compartmental pharmacokinetics of a single oral dose (200 mg) of the anti-epileptic agent, lamotrigine, and its main metabolite, lamotrigine N2-glucuronide, were determined for 10 patients with chronic renal failure of mean estimated creatinine clearance 18 mL min-1 and a control group of 11 healthy volunteers, matched for age and gender. For lamotrigine, there were

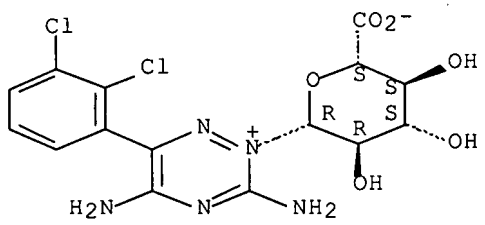
no significant differences in Cmax, tmax, AUC, t1/2,z, CL/F and amount excreted in urine although t1/2,z tended to be longer for the renal failure group with a mean (±s.d.) of 35.9±10.7 h vs 27.8±4.3 h for the control group. For the renal failure group, VZ/F was 18% higher (95% Cl 1% to 39%) compared with controls and CLR was reduced to 61% (95% Cl 46% to 80%) of the control group value. For lamotrigine glucuronide, Cmax was increased 4-fold (95% Cl 3.1 to 5.3) and AUC 7.8-fold (95% Cl 6.0 to 10.1) in the renal failure group compared with controls. CLR was approx. 9-fold lower and apparent t1/2 was increased by 53% (95% Cl 27% to 84%). Concns. of an N2-methylated cardio-active metabolite, previously observed in dogs, were below the limit of detection (2 ng ml-1) of the ASTED/h.p.l.c. assay in the renal failure group as well as controls. These results indicate that impaired renal function will have little effect on the plasma concns. of lamotrigine achieved for a given dosing regimen.

IT 135288-68-5, Lamotrigine N2-glucuronide
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(comparison of lamotrigine pharmacokinetics in patients with chronic renal failure and healthy volunteers)

RN 135288-68-5 CAPLUS

CN 1,2,4-Triazinium, 3,5-diamino-6-(2,3-dichlorophenyl)-2-β-D-glucopyranuronosyl-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L21 ANSWER 25 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:142991 CAPLUS Full-text

DOCUMENT NUMBER: 126:246692

TITLE: Malonate-induced degeneration of basal forebrain cholinergic neurons: attenuation by lamotrigine, MK-801, and 7-nitroindazole

AUTHOR(S): Connop, B. P.; Boegman, R. J.; Beninger, R. J.; Jhamandas, K.

CORPORATE SOURCE: Department of Pharmacology, Queen's University, Kingston, ON, K7L 3N6, Can.

SOURCE: Journal of Neurochemistry (1997), 68(3), 1191-1199
CODEN: JONRA9; ISSN: 0022-3042

PUBLISHER: Lippincott-Raven

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Previously, the authors have reported that intranigral infusions of malonate, an inhibitor of mitochondrial function, lead to the degeneration of the dopaminergic neurons of the nigrostriatal pathway that is mediated, at least in part, through NMDA receptor activation and nitric oxide formation. In the present study, unilateral focal infusions of malonate into the nucleus basalis magnocellularis (nbM) of male Sprague-Dawley rats (weighing 250-300 g)

resulted in a dose-related depletion in ipsilateral cortical and amygdaloid choline acetyltransferase (ChAT) activity. Infusion of a 3 μmol dose of malonate into the nbM of vehicle-treated animals resulted in a 41 and 54% decrease in cortical and amygdaloid ChAT activity, resp. Systemic pretreatment with lamotrigine (16 mg/kg, i.p.) and MK-801 (5 mg/kg, i.p.) attenuated the depletions in cortical and amygdaloid ChAT activity that resulted from an infusion of this dose of malonate into the nbM. Acetylcholinesterase (AChE) histochem. of the nbM following focal infusion of malonate (3 μmol) showed a marked decrease in the number of AChE-pos. neurons that was partially prevented by MK-801 pretreatment. Before examining the role of nitric oxide formation in malonate-induced toxicity, the ability of systemic administration of Nω-nitro-L-arginine (L-NA) to inhibit nitric oxide synthase (NOS) activity in the nbM and cerebellum was investigated. L-NA (2, 10, and 20 mg/kg, i.p.) produced a dose-related inhibition of nbM and cerebellar NOS activity that was maximal following a dose of 10 mg/kg L-NA. This level of NOS inhibition persisted for at least 13 h following L-NA (10 mg/kg) administration. Subsequently, the effect of L-NA pretreatment on malonate toxicity was evaluated. Following pretreatment with L-NA (2 and 10 mg/kg, i.p.), the toxic action of malonate on cortical and amygdaloid ChAT activity was not altered. In addition, infusion of a lower dose of malonate (2 μmol) into the nbM resulted in decreases in cortical and amygdaloid ChAT activity that were not altered by pretreatment with L-NA (2 and 10 mg/kg, i.p.). In 7-nitroindazole (7-NI; 25 and 50 mg/kg, i.p.)-pretreated animals, malonate (3 μmol) produced decreases in cortical and amygdaloid ChAT activity that were attenuated by both doses of 7-NI. Thus, malonate-induced destruction of the basal forebrain cholinergic neurons was attenuated by systemic pretreatment with lamotrigine, MK-801, and 7-NI but not by L-NA.

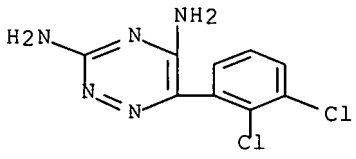
IT 113170-86-8, Lamotrigine isethionate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(malonate-induced degeneration of basal forebrain cholinergic neurons and attenuation by lamotrigine and MK-801 and 7-nitroindazole in relation to enzymes and mechanism of toxicity)

RN 113170-86-8 CAPLUS

CN Ethanesulfonic acid, 2-hydroxy-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

CRN 107-36-8
CMF C2 H6 O4 S

HO—CH2—CH2—SO3H

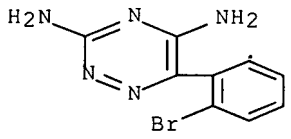
L21 ANSWER 26 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:661668 CAPLUS Full-text
DOCUMENT NUMBER: 125:343452
TITLE: 3,5-Diamino-6-(2-bromophenyl)-1,2,4-triazine dimethanol solvate: an analog of lamotrigine
AUTHOR(S): Janes, Robert W.; Palmer, R. A.
CORPORATE SOURCE: Dep. Crystallography, Birkbeck Coll. Univ. London, London, WC1E 7HX, UK
SOURCE: Acta Crystallographica, Section C: Crystal Structure Communications (1996), C52(10), 2627-2629
CODEN: ACSCEE; ISSN: 0108-2701
PUBLISHER: Munksgaard
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The title compound is monoclinic, space group P21/c, with a 10.516(3), b 12.855(4), c 11.623(2) Å, and β 109.10(2)°; Z = 4, dc = 1.48; R = 0.0496, Rw = 0.0577 for 2048 reflections. Atomic coordinates are given. The structure exhibits marked distortion in its conformation about the common axis of the Ph and triazine rings which may arise from steric hindrance between the Br atom and the π electrons of the triazine ring. An extensive network of H bonds maintains the crystal structure which has one analog mol. and two MeOH solvent mols. per asym. unit.

IT 183485-04-3, 3,5-Diamino-6-(2-bromophenyl)-1,2,4-triazine compound with methanol (1:2)
RL: PRP (Properties)
(crystal structure of)
RN 183485-04-3 CAPLUS
CN Methanol, compd. with 6-(2-bromophenyl)-1,2,4-triazine-3,5-diamine (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 77668-49-6
CMF C9 H8 Br N5



CM 2

CRN 67-56-1
CMF C H4 O

H3C—OH

L21 ANSWER 27 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:616102 CAPLUS Full-text
DOCUMENT NUMBER: 125:256936
TITLE: Moisture-Dependent Crystallization of Amorphous Lamotrigine Mesylate
AUTHOR(S): Schmitt, E.; Davis, C. W.; Long, S. T.
CORPORATE SOURCE: Glaxo Wellcome Inc., Research Triangle Park, NC, 27709, USA
SOURCE: Journal of Pharmaceutical Sciences (1996), 85(11), 1215-1219
CODEN: JPMSAE; ISSN: 0022-3549
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

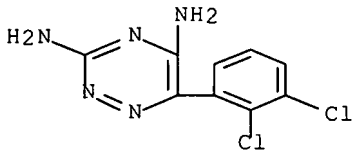
AB A com. available computer-controlled vacuum moisture balance was used for determining moisture sorption isotherms of freeze-dried and spray-dried lamotrigine mesylate and freeze-dried drug product containing mannitol. The presence or absence of desorption hysteresis and the characteristics of the weight-vs.-time profile as a sample was exposed to a defined relative humidity ramp were sensitive indicators of moisture-induced crystallization Combination of the moisture sorption data with polarized light microscopy, DSC, and x-ray powder diffraction provided qual. verification of the crystallization with <50 mg of sample. The normalized water loss during crystallization was used to detect as little as 2% amorphous content in phys. mixts. of amorphous and crystalline lamotrigine mesylate. Moisture sorption, water plasticization, and crystallization properties of amorphous forms prepared by spray drying and freeze drying were nearly identical. Cofreeze-drying lamotrigine mesylate with D-mannitol resulted in a mixture of amorphous lamotrigine mesylate with properties similar to those of spray-dried or freeze-dried materials and crystalline D-mannitol. The amount of water needed for crystallization over a time scale observable in the moisture balance was considerably more than the amount needed to lower the glass transition temperature of the sample to the operating temperature of the instrument. This result illustrated the importance of time scale effects in determining critical moisture levels for crystallization from the amorphous state.

IT 181362-54-9
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(moisture-dependent crystallization of amorphous lamotrigine mesylate)

RN 181362-54-9 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)-, methanesulfonate (9CI) (CA INDEX NAME)

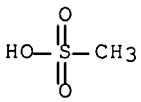
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

CRN 75-75-2
CMF C H4 O3 S

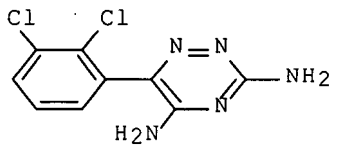


L21 ANSWER 28 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:548552 CAPLUS Full-text
DOCUMENT NUMBER: 125:195694
TITLE: Preparation of lamotrigine.
INVENTOR(S): Winter, Raymond Geoffrey; Sawyer, David Alan; Germain, Andrew
PATENT ASSIGNEE(S): Wellcome Foundation Limited, UK
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

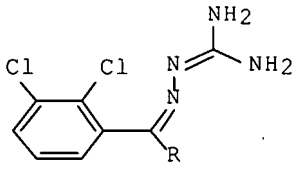
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9620934	A1	19960711	WO 1995-GB3048	19951229 <--
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9643115	A	19960724	AU 1996-43115	19951229 <--
EP 800520	A1	19971015	EP 1995-941817	19951229 <--
EP 800520	B1	20020619		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
HU 77346	A2	19980330	HU 1997-1867	19951229 <--
HU 224688	B1	20051228		
JP 11501007	T	19990126	JP 1995-520803	19951229 <--
RU 2145602	C1	20000220	RU 1997-112881	19951229 <--
AT 219487	T	20020715	AT 1995-941817	19951229 <--

PT 800520	T	20021129	PT 1995-941817		19951229 <--
ES 2177672	T3	20021216	ES 1995-941817		19951229 <--
FI 9702719	A	19970827	FI 1997-2719		19970624 <--
US 5912345	A	19990615	US 1997-836153		19970625 <--
PRIORITY APPLN. INFO.:			GB 1994-26439	A	19941230 <--
			GB 1994-26447	A	19941230 <--
			WO 1995-GB3048	W	19951229 <--

OTHER SOURCE(S): CASREACT 125:195694; MARPAT 125:195694
GI



I



II

AB Lamotrigine (I) was prepared by irradiation of (II; R = CN, CONH2) with UV or visible radiation in an organic solvent, or, when R = CN, by heating. Thus, II (R = CN) was refluxed in 1-propanol under irradiation from a medium pressure Hg lamp for 8 h to give 73% lamotrigine.

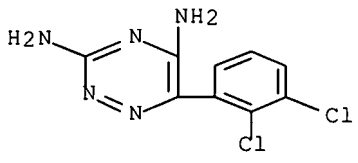
IT 113170-86-8P, Lamotrigine isethionate
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of lamotrigine)

RN 113170-86-8 CAPLUS

CN Ethanesulfonic acid, 2-hydroxy-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

CRN 107-36-8
CMF C2 H6 O4 S

HO—CH_2—CH_2—SO_3H

L21 ANSWER 29 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:546365 CAPLUS Full-text
DOCUMENT NUMBER: 125:195693
TITLE: Preparation of lamotrigine.
INVENTOR(S): Lee, Grahame Roy
PATENT ASSIGNEE(S): Wellcome Foundation Limited, UK
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9620935	A1	19960711	WO 1995-GB3049	19951229 <--
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9643116	A	19960724	AU 1996-43116	19951229 <--
EP 800521	A1	19971015	EP 1995-941818	19951229 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
HU 77347	A2	19980330	HU 1997-1875	19951229 <--
JP 11507011	T	19990622	JP 1995-520618	19951229 <--
RU 2162081	C2	20010120	RU 1997-112921	19951229 <--
FI 9702720	A	19970827	FI 1997-2720	19970624 <--
US 5925755	A	19990720	US 1997-836152	19970625 <--

PRIORITY APPLN. INFO.: GB 1994-26448 A 19941230 <--
WO 1995-GB3049 W 19951229 <--

AB Lamotrigine, 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (I), is prepared by treating 6-(2,3-dichlorophenyl)-5-chloro-3-thiomethyl-1,2,4-triazine (II) with NH3. Thus, II (preparation given) was heated with ethanolic NH3 in a sealed tube at 180° and 280 psi for 72 h to give I.

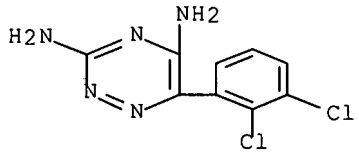
IT 113170-86-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of lamotrigine)

RN 113170-86-8 CAPLUS

CN Ethanesulfonic acid, 2-hydroxy-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



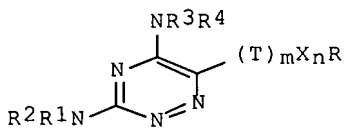
CM 2

CRN 107-36-8
CMF C2 H6 O4 S

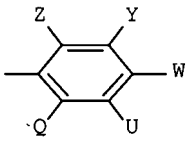
L21 ANSWER 30 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:248959 CAPLUS Full-text
DOCUMENT NUMBER: 125:10859
TITLE: 6-Substituted-3,5-diamino-1,2,4-triazines as insecticides
INVENTOR(S): Peake, Clinton J.; Cullen, Thomas G.
PATENT ASSIGNEE(S): FMC Corp., USA
SOURCE: U.S., 15 pp., Cont.-in-part of U. S. Ser. No. 338,288, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
US 5502054	A	19960326	US 1995-424144		19950418	<--
PRIORITY APPLN. INFO.:			US 1995-424144	B2	19950418	<--
			US 1994-338288	B1	19941110	<--
			US 1994-289080		19940811	<--

OTHER SOURCE(S): MARPAT 125:10859
GI



I

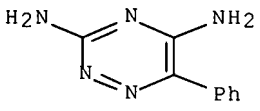


II

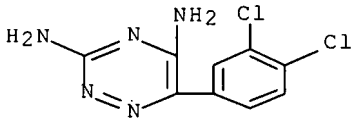
AB An insecticidal composition is claimed, comprising, in admixt. with an agriculturally acceptable carrier, an insecticidally effective amount of a

1,2,4-triazine compound of the formula I wherein m is 1 to 12; n is 0 or 1; T is CH2, CH:CH, or C.tplbond.C; X is Si(CH3)2, C(CH3)2, CH(CH3), or O; and R is Me, vinyl, cyclopentyl, Ph, naphthyl, or a substituted Ph of the formula II wherein Q is hydrogen or chloro; U is hydrogen, chloro, trifluoromethyl, Ph, or 4-fluorophenyl; W is hydrogen, Et, chloro, trifluoromethyl, or propylsulfonyl; Y is hydrogen, chloro, bromo or trifluoromethyl; and Z is hydrogen; R1, R2, R3, and R4 are independently selected from the group consisting of hydrogen, CH3, C2H5, or C(O)R5, where R5 is straight or branched chain lower alkyl of one to three carbon atoms, CH2OCH2CH3, CH2OCH2CH2CH3, CH2CH2OCH3, or CH2CH2OCH2CH3; with the proviso that when T is alkylene or acetylene, m must be 1; and agriculturally acceptable salts thereof. Thus, e.g., 4,4-dimethyl-4- silapentanol was oxidized to 4,4-dimethyl-4-silapentanoic acid, converted to the acid chloride and then to 4,4-dimethyl-4-silapentanoyl cyanide; cyclization with aminoguanidine afforded 3,5-diamino-6-(3,3-dimethyl-3- silabutyl)-1,2,4-triazine [I; R1-R4 = H; (T)mXnR = (CH2)2SiMe3] which exhibited 90, 95, and 95% control, resp., of tobacco budworm, cabbage looper, and beet armyworm at 3000 ppm.

IT 6719-24-0P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(6-substituted-3,5-diamino-1,2,4-triazines as insecticides)
RN 6719-24-0 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-phenyl- (9CI) (CA INDEX NAME)

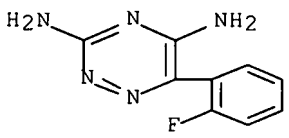


IT 36518-85-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(6-substituted-3,5-diamino-1,2,4-triazines as insecticides)
RN 36518-85-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(3,4-dichlorophenyl)- (9CI) (CA INDEX NAME)



L21 ANSWER 31 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:791730 CAPLUS Full-text
DOCUMENT NUMBER: 123:284928
TITLE: Practical limitations observed using the AM1, MNDO and MINDO/3 semi-empirical methods for charge calculation and structure optimization in 1,2,4-triazine ring-containing compounds
AUTHOR(S): Janes, Robert W.; Palmer, Rex A.
CORPORATE SOURCE: Department of Crystallography, Birkbeck College,

University of London, London, WC1E 7HX, UK
SOURCE: THEOCHEM (1995), 339, 95-101
CODEN: THEODJ; ISSN: 0166-1280
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An investigation employing the semi-empirical AM1, MNDO and MINDO/3 methods in the program package AMPAC to calculate both electronic charge distribution and structure optimization on compds. containing a 1,2,4-triazine ring moiety has been undertaken. Significant errors are found in the results obtained, when compared with known crystallog. data, in bond lengths, bond angles and dihedral angles of the optimized structures. Also from crystallog. data the charges calculated for the exptl. determined and optimized structures are shown to be inaccurate. These results severely question the use of these semi-empirical approaches in heteroarom. compds. containing nitrogen-nitrogen ring bonds.
IT 35857-42-2, 1,2,4-Triazine-3,5-diamine, 6-(2-fluorophenyl)-
RL: PRP (Properties)
(semi-empirical methods for charge calcn. and structure optimization in 1,2,4-triazine ring-containing compds.)
RN 35857-42-2 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



L21 ANSWER 32 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:499316 CAPLUS Full-text
DOCUMENT NUMBER: 123:699
TITLE: Cerebroprotective effect of lamotrigine after focal ischemia in rats
AUTHOR(S): Smith, Stuart E.; Meldrum, Brian S.
CORPORATE SOURCE: Department of Neurology, Institute of Psychiatry, Denmark Hill, SE5 8AF, UK
SOURCE: Stroke (1995), 26(1), 117-22
CODEN: SJCCA7; ISSN: 0039-2499
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Glutamate receptor antagonists are protective in animal models of focal cerebral ischemia. Lamotrigine (3,5-diamino-6-[2,3-dichlorophenyl]-1,2,4-triazine) is an anticonvulsant drug that blocks voltage-gated sodium channels and inhibits the ischemia-induced release of glutamate. The cerebroprotective effect of lamotrigine (as the isethionate salt) after middle cerebral artery occlusion was described in rats. Neurol. deficit and infarct volume (visualized by the lack of reduction of 2,3,5- triphenyltetrazolium chloride) 24 h after permanent left middle cerebral artery occlusion were studied in Fischer rats (n=8 per group per dose). Lamotrigine at 20 mg/kg i.v. over 10 min administered immediately after middle cerebral artery occlusion reduced total infarct volume by 31% and cortical infarct volume by 52%. Lamotrigine at 8 mg/kg i.v. over 10 min reduced cortical infarct volume by 38%. Lamotrigine at 50 mg/kg i.v. for 10 min was not cerebroprotective and induced a decrease of 29±15 mm Hg in mean arterial blood pressure (P<.05, n=8). The

optimum dose of lamotrigine (20 mg/kg i.v. over 10 min) when administered with a 1-h delay after middle cerebral artery occlusion reduced cortical infarct volume by 41%. Lamotrigine (20 mg/kg i.v. over 10 min) with a 2-h delay after middle cerebral artery occlusion was ineffective. Neurol. deficits after 24 h were improved after immediate treatment with lamotrigine at 20 mg/kg i.v. over 10 min. The cerebroprotective effect of lamotrigine in rats is limited to a narrow dose range between 8 and 20 mg/kg. Lamotrigine or analogous compds. may be useful when given shortly after the onset of stroke.

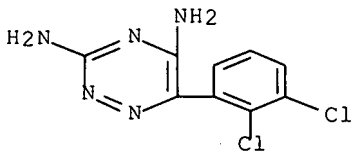
IT 158879-27-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cerebroprotective effect of lamotrigine after focal ischemia)

RN 158879-27-7 CAPLUS

CN Ethanesulfonic acid, 2-hydroxy-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (9CI) (CA INDEX NAME)

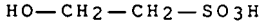
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

CRN 107-36-8
CMF C2 H6 O4 S



L21 ANSWER 33 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:491380 CAPLUS Full-text
DOCUMENT NUMBER: 122:278663
TITLE: A lamotrigine analog: 3,5-diamino-6-(2-fluorophenyl)-1,2,4-triazine methanol solvate
AUTHOR(S): Janes, Robert W.; Palmer, R. A.
CORPORATE SOURCE: Dep. Crystallography, Birkbeck Coll., London, WC1E 7HX, UK
SOURCE: Acta Crystallographica, Section C: Crystal Structure Communications (1995), C51(3), 440-2
CODEN: ACSCEE; ISSN: 0108-2701
PUBLISHER: Munksgaard
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The crystal of the title compound, C9H8FN5.MeOH, contains two conformers of the triazine mol. in the asym. unit, each with significantly distinct dihedral angles between their resp. Ph and triazine rings [50.8(1) and 125.0(1)°]. These two conformers exhibit significant differences in certain bond lengths and angles which may arise because of their different dihedral angles. An extensive H-bonding network maintains the crystal structure which also incorporates two solvent MeOH mols. Crystallog. data and atomic coordinates are given.

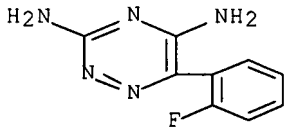
IT 162716-46-3
RL: PRP (Properties)
(crystal structure of)

RN 162716-46-3 CAPLUS

CN Methanol, compd. with 6-(2-fluorophenyl)-1,2,4-triazine-3,5-diamine (1:1) (9CI) (CA INDEX NAME)

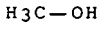
CM 1

CRN 35857-42-2
CMF C9 H8 F N5



CM 2

CRN 67-56-1
CMF C H4 O



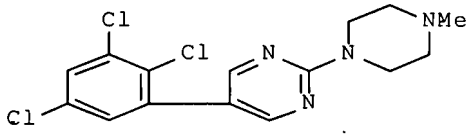
L21 ANSWER 34 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:35265 CAPLUS Full-text
DOCUMENT NUMBER: 122:160666
TITLE: Pyrimidine, pyridine, pteridinone and indazole derivatives as enzyme inhibitors
INVENTOR(S): Bigham, Eric Cleveland; Reinhard, John Frederick, Jr.; Moore, Philip Keith; Babbedge, Rachel Cecilia; Knowles, Richard Graham; Nobbs, Malcolm Stuart; Bull, Donald
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

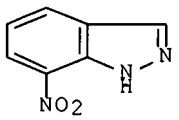
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9414780	A1	19940707	WO 1993-GB2556	19931215 <--
W: AU, CA, CZ, JP, KR, KZ, NO, NZ, PL, RU, UA, US, UZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9457045	A	19940719	AU 1994-57045	19931215 <--
EP 674627	A1	19951004	EP 1994-902868	19931215 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08504798	T	19960521	JP 1993-514909	19931215 <--
ZA 9309480	A	19950619	ZA 1993-9480	19931217 <--
US 5459158	A	19951017	US 1993-168246	19931217 <--
PRIORITY APPLN. INFO.:			GB 1992-26377 A	19921218 <--
			GB 1993-3221 A	19930218 <--
			WO 1993-GB2556 W	19931215 <--

OTHER SOURCE(S): MARPAT 122:160666

GI



I



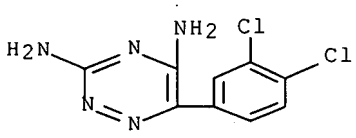
II

AB The use of a compound which binds at the tetrahydrobiopterin site of NO synthase for the treatment of conditions where there is an advantage in inhibiting neuronal NO synthase with little or no inhibition of endothelial NO synthase is disclosed. Pharmaceutical formulations comprising such compds., i.e., pyridinediamines, pyrimidinediamines and indazole derivs., and processes for their preparation are also disclosed. An example compound, 1-methyl-4-[5-(2,3,5-trichlorophenyl)-2-pyrimidinyl]-1- methylpiperazine (I) inhibited NO synthase in vitro (IC50 = 5.0 μM). Another compound, 7-nitroindazole (II), inhibited NO synthase in mice (IC50 = 1 μM).

IT 36518-85-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(neuronal NO synthase inhibitor)

RN 36518-85-1 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(3,4-dichlorophenyl)- (9CI) (CA INDEX NAME)



L21 ANSWER 35 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1994:663729 CAPLUS Full-text

DOCUMENT NUMBER: 121:263729

TITLE: Use of triazine compounds for the treatment of memory and learning disorders

INVENTOR(S): Baxter, Martin George
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9421260	A1	19940929	WO 1994-GB559	19940318 <--
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9462176	A	19941011	AU 1994-62176	19940318 <--
ZA 9401938	A	19950918	ZA 1994-1938	19940318 <--
EP 689439	A1	19960103	EP 1994-909263	19940318 <--
EP 689439	B1	20010124		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08507782	T	19960820	JP 1994-520807	19940318 <--
IL 109034	A	19981206	IL 1994-109034	19940318 <--
AT 198831	T	20010215	AT 1994-909263	19940318 <--
ES 2153854	T3	20010316	ES 1994-909263	19940318 <--
PT 689439	T	20010531	PT 1994-909263	19940318 <--
US 5866597	A	19990202	US 1997-900868	19970725 <--
GR 3035528	T3	20010629	GR 2001-400367	20010308 <--
PRIORITY APPLN. INFO.:			GB 1993-5693 A	19930319 <--
			WO 1994-GB559 W	19940318 <--
			US 1996-535140 B1	19960328 <--

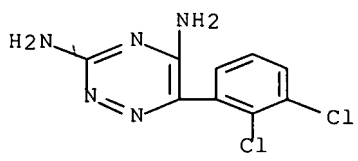
AB 3,5-Diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (I) and its pharmaceutically acceptable acid addition salts can be used to treat impaired memory and learning disorders. Therapeutic effects of I were demonstrated in a scopolamine-induced mouse model of memory deficit and compared with those of ondansetron HCl and piracetam. A tablet containing 150 mg I was also formulated.

IT 158879-27-7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(agent for treatment of memory and learning disorders)

RN 158879-27-7 CAPLUS
CN Ethanesulfonic acid, 2-hydroxy-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (9CI) (CA INDEX NAME)

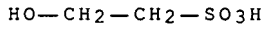
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

CRN 107-36-8
CMF C2 H6 O4 S



L21 ANSWER 36 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:663728 CAPLUS Full-text
DOCUMENT NUMBER: 121:263728
TITLE: Use of triazine compounds as anxiolytics
INVENTOR(S): Critchley, Martyn Alan Edwin
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9421261	A1	19940929	WO 1994-GB560	19940318 <--
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9462177	A	19941011	AU 1994-62177	19940318 <--
ZA 9401939	A	19950918	ZA 1994-1939	19940318 <--
EP 689440	A1	19960103	EP 1994-909264	19940318 <--
EP 689440	B1	20000531		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08507783	T	19960820	JP 1994-520808	19940318 <--
JP 3633618	B2	20050330		
AT 193446	T	20000615	AT 1994-909264	19940318 <--
ES 2147232	T3	20000901	ES 1994-909264	19940318 <--
PT 689440	T	20001031	PT 1994-909264	19940318 <--
US 5658905	A	19970819	US 1995-535139	19950918 <--
GR 3033941	T3	20001130	GR 2000-401626	20000712 <--
PRIORITY APPLN. INFO.:			GB 1993-5692 A	19930319 <--
			WO 1994-GB560 W	19940318 <--

AB 3,5-Diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (I) and its pharmaceutically acceptable acid addition salts can be used to treat anxiety and anxiety disorders. For example, an anxiolytic effect of I-isethionate was demonstrated with Vogel conflict model in rats. A tablet containing 150 mg I was also formulated.

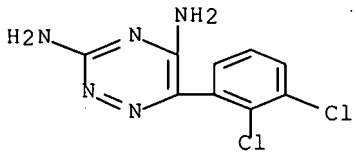
IT 158879-27-7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(agent for treatment of anxiety disorders)

RN 158879-27-7 CAPLUS

CN Ethanesulfonic acid, 2-hydroxy-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (9CI) (CA INDEX NAME)

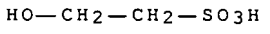
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

CRN 107-36-8
CMF C2 H6 O4 S



L21 ANSWER 37 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:124865 CAPLUS Full-text
DOCUMENT NUMBER: 120:124865
TITLE: Use of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine isethionate for the treatment and prevention of dependence on, tolerance to, and sensitization to drugs
INVENTOR(S): Nakamura-Craig, Meire
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9325207	A1	19931223	WO 1993-GB1243	19930611 <--
W: AU, CA, CZ, GB, JP, KR, NO, NZ, PL, RU, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9343452	A	19940104	AU 1993-43452	19930611 <--
AU 688729	B2	19980319		
EP 644763	A1	19950329	EP 1993-913346	19930611 <--
EP 644763	B1	19970122		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
GB 2282326	A	19950405	GB 1994-23697	19930611 <--
JP 07507790	T	19950831	JP 1993-501281	19930611 <--
AT 147980	T	19970215	AT 1993-913346	19930611 <--
ES 2097516	T3	19970401	ES 1993-913346	19930611 <--
CZ 284061	B6	19980812	CZ 1994-3128	19930611 <--

IL 105986	A	19981206	IL 1993-105986		19930611 <--
SK 279730	B6	19990211	SK 1994-1534		19930611 <--
HR 930964	B1	20000630	HR 1993-964		19930611 <--
JP 3439211	B2	20030825	JP 1994-501281		19930611 <--
US 5801171	A	19980901	US 1994-347480		19941206 <--
NO 9404790	A	19941209	NO 1994-4790		19941209 <--
PRIORITY APPLN. INFO.:			GB 1992-12495	A	19920612 <--
			GB 1993-8654	A	19930427 <--
			WO 1993-GB1243	A	19930611 <--

AB 3,5-Diamino-6-(2,3-dichlorophenyl)-1,2,4,-triazine (I) and its pharmaceutically and veterinarily acceptable salts (especially the ethionate) have activity in (a) preventing or reducing dependence on, and (b) preventing or reducing tolerance or reverse tolerance to, a dependence-inducing agent such as an opioid, a central nervous system depressant, a psychostimulant, or nicotine. Thus, I (5 mg/kg orally twice a day during morphine habituation) attenuated the development of morphine tolerance in rats without affecting the analgesic effect of morphine in the tail-flick test.

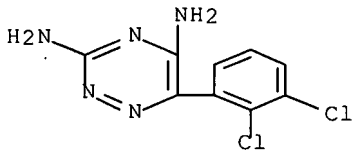
IT 113170-86-8
RL: BIOL (Biological study)
(drug dependence and sensitization and tolerance prevention and treatment with)

RN 113170-86-8 CAPLUS

CN Ethanesulfonic acid, 2-hydroxy-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (1:1) (9CI) (CA INDEX NAME)

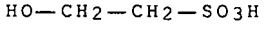
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

CRN 107-36-8
CMF C2 H6 O4 S



L21 ANSWER 38 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:617428 CAPLUS Full-text
DOCUMENT NUMBER: 119:217428
TITLE: Use of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine for the treatment of pain and edema
INVENTOR(S): Nakamura-Craig, Meire; Leach, Michael John

PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

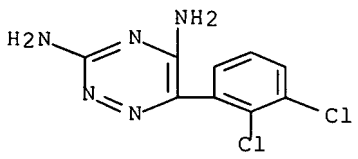
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9316700	A1	19930902	WO 1993-GB341	19930218 <--
W: AU, CA, GB, JP, KR, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9335092	A	19930913	AU 1993-35092	19930218 <--
AU 684711	B2	19980108		
EP 626851	A1	19941207	EP 1993-904225	19930218 <--
EP 626851	B1	20010822		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07503968	T	19950427	JP 1993-514628	19930218 <--
JP 3713271	B2	20051109		
IL 104775	A	19970218	IL 1993-104775	19930218 <--
AT 204476	T	20010915	AT 1993-904225	19930218 <--
ES 2162813	T3	20020116	ES 1993-904225	19930218 <--
PT 626851	T	20020228	PT 1993-904225	19930218 <--
CA 2129043	C	20040127	CA 1993-2129043	19930218 <--
GB 2277265	A	19941026	GB 1994-14348	19940715 <--
GB 2277265	B	19960110		
US 5712277	A	19980127	US 1996-680111	19960715 <--
GR 3036958	T3	20020131	GR 2001-401827	20011022 <--

PRIORITY APPLN. INFO.:	GB 1992-3483	A	19920219 <--
	WO 1993-GB341	A	19930218 <--
	US 1994-284497	A1	19940804 <--

AB The title compound (I) is useful in medicaments for the prevention or treatment of pain or edema. A tablet formulation containing I is given. I was tested in rats.

IT 84057-84-1, 3,5-Diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine
113170-86-8
RL: BIOL (Biological study)
(edema or pain treatment with)

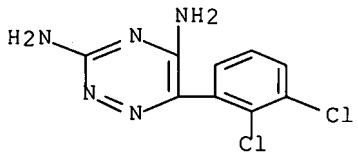
RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (CA INDEX NAME)



RN 113170-86-8 CAPLUS
CN Ethanesulfonic acid, 2-hydroxy-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (1:1) (9CI) (CA INDEX NAME)

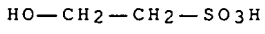
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5

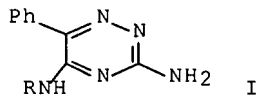


CM 2

CRN 107-36-8
CMF C2 H6 O4 S



L21 ANSWER 39 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:124498 CAPLUS Full-text
DOCUMENT NUMBER: 118:124498
TITLE: Synthesis of 3-amino-5-substituted phenylamino-6-phenyl-1,2,4-triazines
AUTHOR(S): Lu, Zhonge; Wan, Jun; Chen, Keqian
CORPORATE SOURCE: Dep. Chem., Suzhou Univ., Suzhou, 215006, Peop. Rep. China
SOURCE: Youji Huaxue (1992), 12(6), 605-7
CODEN: YCHHDX; ISSN: 0253-2786
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 118:124498
GI

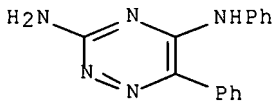


I

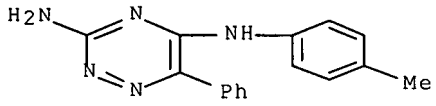
AB A new synthetic method of 3-amino-5-substituted phenylamino-6-phenyl-1,2,4-triazines was reported. Benzoylthioformanilides were first condensed with aminoguanidine dihydrochloride in slightly acidic medium, then refluxed in alkaline medium (pH 8.apprx.9) to give title compds. by the elimination of hydrogen sulfide. Nine 1,2,4-triazines I (R = Ph, substituted Ph) were synthesized by this reaction in good yields.

IT 142706-34-1 146330-32-7 146330-33-8
146330-34-9 146330-35-0 146330-36-1
146330-37-2 146330-38-3 146330-39-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation of, with benzoylthioformanilide)

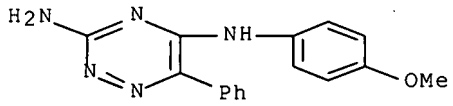
RN 142706-34-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, N5,6-diphenyl- (9CI) (CA INDEX NAME)



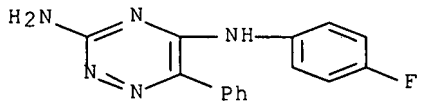
RN 146330-32-7 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, N5-(4-methylphenyl)-6-phenyl- (9CI) (CA INDEX NAME)



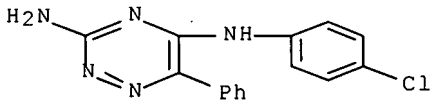
RN 146330-33-8 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, N5-(4-methoxyphenyl)-6-phenyl- (9CI) (CA INDEX NAME)



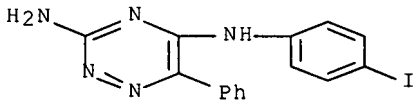
RN 146330-34-9 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, N5-(4-fluorophenyl)-6-phenyl- (9CI) (CA INDEX NAME)



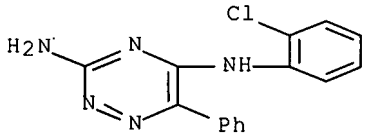
RN 146330-35-0 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, N5-(4-chlorophenyl)-6-phenyl- (9CI) (CA INDEX NAME)



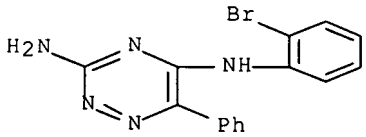
RN 146330-36-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, N5-(4-iodophenyl)-6-phenyl- (9CI) (CA INDEX NAME)



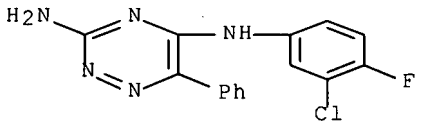
RN 146330-37-2 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, N5-(2-chlorophenyl)-6-phenyl- (9CI) (CA INDEX NAME)



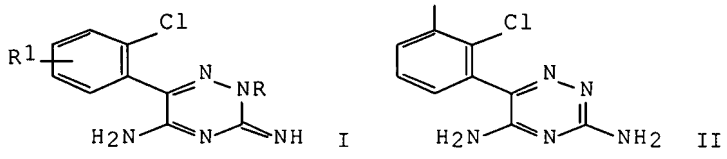
RN 146330-38-3 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, N5-(2-bromophenyl)-6-phenyl- (9CI) (CA INDEX NAME)



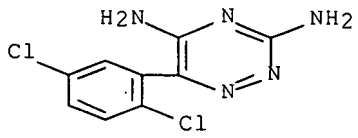
RN 146330-39-4 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, N5-(3-chloro-4-fluorophenyl)-6-phenyl- (9CI) (CA INDEX NAME)



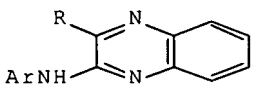
L21 ANSWER 40 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:651326 CAPLUS Full-text
DOCUMENT NUMBER: 117:251326
TITLE: Synthesis of analogs of BW A256C, a novel antiarrhythmic agent
AUTHOR(S): Zheng, Weiping; Bai, Donglu
CORPORATE SOURCE: Shanghai Inst. Mater. Med., Chin. Acad. Sci., Shanghai, 200031, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (1992), 23(4), 163-4 .
CODEN: ZYGZEA; ISSN: 1001-8255
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
GI

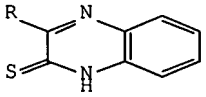


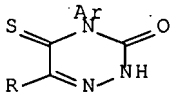
AB The title compds. [I; R = Me2CH, Et; R1 = Cl], more effective than BW A256C, are prepared Refluxing a solution of EtI and II in Me2CO gave 24.8% I (R = Et, R1 = 3-Cl), which was .apprx.3 times more effective than BWA 256C at 1 mg/kg i.v. in rats.
IT 77668-43-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(Ethylation of, in preparation of antiarrhythmic agent)
RN 77668-43-0 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,5-dichlorophenyl)- (9CI) (CA INDEX NAME)



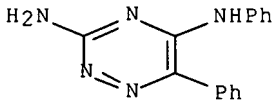
L21 ANSWER 41 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:511576 CAPLUS Full-text
DOCUMENT NUMBER: 117:111576
TITLE: New heterocycle forming reactions of acyl thioformanilides
AUTHOR(S): Lu, Zhonge; Sun, Daqing; Xu, Tianlin; Wan, Jun; Xu, Lecun; Chen, Keqian
CORPORATE SOURCE: Dep. Chem., Suzhou Univ., Suzhou, 215006, Peop. Rep. China
SOURCE: Organic Preparations and Procedures International (1992), 24(3), 358-62
CODEN: OPPIAK; ISSN: 0030-4948
DOCUMENT TYPE: Journal
LANGUAGE: English
GI


I


III

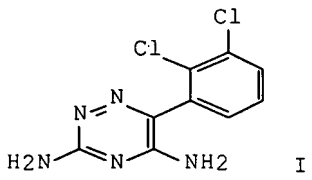

IV

AB Quinoxalines I (R = Ph, CMe3, Ar = Ph, 4-MeOC6H4, 2-MeC6H4, 4-O2NC6H4, etc.) were prepared by cyclocondensation of RCOCSNHAr (II) with 1,2-(H2N)2C6H4 in pyridine at reflux. When II (R = Ar = Ph) reacted with 1,2-(H2N)2C6H4 in MeOH/HOAc at room temperature quinoxalinethione III was obtained. II condensed with semicarbazide in EtOH to give the corresponding semicarbazones which were cyclized to give triazines IV in 81-87% yields.
IT 142706-34-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 142706-34-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, N5,6-diphenyl- (9CI) (CA INDEX NAME)



L21 ANSWER 42 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:227574 CAPLUS Full-text
DOCUMENT NUMBER: 116:227574
TITLE: In vitro N-glucuronidation of a novel antiepileptic drug, lamotrigine, by human liver microsomes
AUTHOR(S): Magdalou, Jacques; Herber, Regine; Bidault, Roselyne; Siest, Gerard
CORPORATE SOURCE: Cent. Med., CNRS, Nancy, 5400, Fr.
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1992), 260(3), 1166-73

CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

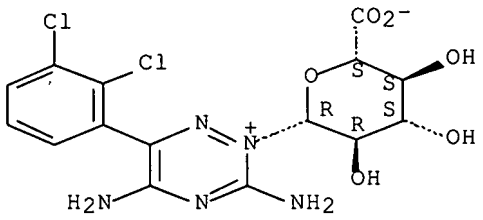
AB The metabolism of the antiepileptic drug lamotrigine (I) was characterized in human liver microsomes. For this purpose, an HPLC method allowing the separation of lamotrigine glucuronide from the parent compound, and the quantitation of the glucuronide, was developed. The drug undergoes glucuronidation on the 2-nitrogen atom of the triazine ring, leading to a quaternary ammonium-linked glucuronide. This metabolite was pos. identified from its hydrolysis by β-glucuronidase and its associated radioactivity when UDP-[U-14C] glucuronic acid was used as the cosubstrate. Structural confirmation of the glucuronide was finally obtained by HPLC-mass spectrometry, using a thermospray interface. The reaction proceeded with an apparent Vmax of 0.65 nmol/min/mg and Km of 2.56 mM. The average value of lamotrigine glucuronidation in four human samples of transplantable liver was 0.43 nmol/min/mg, thus indicating a large interindividual variation. An interspecies comparison of hepatic lamotrigine glucuronidation (human, rabbit, rat, monkey) revealed that the rate of glucuronidation was low. Of all the species considered, humans glucuronidated the drug to the greatest extent, with a specific activity of 2-fold higher than that observed in rabbit liver microsomes. In contrast, the activity was >20 times lower in monkey (0.019 nmol/min/mg) and at the limit of detection in rat liver microsomes. However, in this species, phenobarbital treatment enhanced lamotrigine glucuronidation slightly (0.017 nmol/min/mg). Among drugs that undergo quaternary ammonium-linked glucuronidation, chlorpromazine, but not imipramine, amitriptyline and cyproheptadine, inhibited the glucuronidation of lamotrigine in vitro (IC50 of 5.0 + 10-4M). The reaction was strongly inhibited by 17β-hydroxysteroids testosterone, ethynylestradiol and norethindrone in both male and female human liver microsomes. Testosterone and ethynylestradiol competitively inhibited lamotrigine glucuronidation with similar apparent Ki values (62 μM), thus suggesting that the drug and the hormones were substrates of the same mol. form(s) of UDP-glucuronosyltransferase.

IT 135288-68-5
RL: FORM (Formation, nonpreparative)
(formation of, by human liver microsomes, kinetics and UDP-glucuronosyltransferase isoform in)

RN 135288-68-5 CAPLUS

CN 1,2,4-Triazinium, 3,5-diamino-6-(2,3-dichlorophenyl)-2-β-D-glucopyranuronosyl-, inner salt (9CI) (CA INDEX NAME)

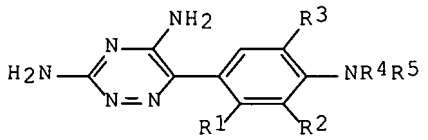
Absolute stereochemistry.



L21 ANSWER 43 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:128970 CAPLUS Full-text
DOCUMENT NUMBER: 116:128970
TITLE: Preparation of 6-aminophenyl-3,5-diamino-1,2,4-triazines as neuroprotective agents
INVENTOR(S): Leach, Michael John; Nobbs, Malcolm Stuart
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 459829	A1	19911204	EP 1991-304962	19910531 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 9104158	A	19930301	ZA 1991-4158	19910530 <--
CA 2043642	A1	19911202	CA 1991-2043642	19910531 <--
FI 9102622	A	19911202	FI 1991-2622	19910531 <--
AU 9178099	A	19911205	AU 1991-78099	19910531 <--
AU 630811	B2	19921105		
HU 60726	A2	19921028	HU 1991-1827	19910531 <--
JP 06025193	A	19940201	JP 1991-235335	19910531 <--

PRIORITY APPLN. INFO.: GB 1990-12312 A 19900601 <--
OTHER SOURCE(S): MARPAT 116:128970
GI

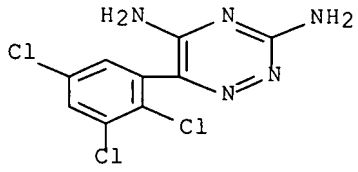


I

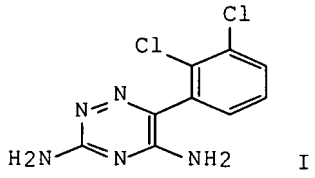
AB Title compds. (I; 1 of R1-R3 = Cl and the others = H or Cl; R4, R5 = H, alkyl) were prepared Thus, 2,5,3-Cl2(H2N)C6H2CO2H was converted in 3 steps to 2,3,5-Cl3C6H2COCN which was cyclocondensed with H2NC(:NH)NHNH2 and the product nitrated to give, after reduction, I (R1-R3 = Cl, R4 = R5 = H). The latter had IC50 of <10 μM against glutamate release from rat brain slices.

IT 77668-56-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(preparation and reaction of, in preparation of neuroprotectants)
RN 77668-56-5 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3,5-trichlorophenyl)- (9CI) (CA INDEX NAME)



L21 ANSWER 44 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:33813 CAPLUS Full-text
DOCUMENT NUMBER: 116:33813
TITLE: Analysis of lamotrigine and lamotrigine 2-N-glucuronide in guinea pig blood and urine by reserved-phase ion-pairing liquid chromatography
AUTHOR(S): Sinz, Michael W.; Remmel, Rory P.
CORPORATE SOURCE: Dep. Med. Chem., Univ. Minnesota, Minneapolis, MN, 55455, USA
SOURCE: Journal of Chromatography (1991), 571(1-2), 217-30
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Lamotrigine (I)is an investigational anticonvulsant drug undergoing clin. trials. A simultaneous assay was developed to quantitate lamotrigine and its major metabolite, lamotrigine 2-N-glucuronide, from guinea pig whole blood. The extraction procedure and reversed-phase high-performance liquid chromatog. (HPLC) assay employed sodium dodecylsulfate (SDS) as an ion-pairing reagent to selectively sep. lamotrigine and lamotrigine 2-N-glucuronide from endogenous blood components, other anticonvulsant drugs, and their metabolites. The mobile phase was composed of acetonitrile-50 mM phosphoric acid (pH 2.2) containing 10 mM SDS (33:67, volume/volume), and components were detected at 277 nm. Sep. assays for lamotrigine and its glucuronide in urine were developed. In order to quantitate low levels of lamotrigine in guinea pig urine, lamotrigine was extracted with tert-Bu Me ether-Et acetate (1:1). For

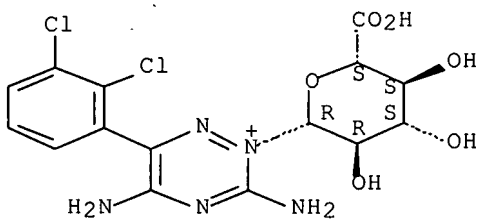
the determination of lamotrigine 2-N-glucuronide, urine was diluted with an SDS-phosphoric acid buffer (1:4) and injected directly onto the HPLC system.

IT 133310-19-7
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in blood and urine by HPLC)

RN 133310-19-7 CAPLUS

CN 1,2,4-Triazinium, 3,5-diamino-6-(2,3-dichlorophenyl)-2-β-D-glucopyranuronosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L21 ANSWER 45 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1991:573974 CAPLUS Full-text

DOCUMENT NUMBER: 115:173974

TITLE: Use of thermospray liquid chromatography-mass spectrometry to aid in the identification of urinary metabolites of a novel antiepileptic drug, Lamotrigine

AUTHOR(S): Doig, M. V.; Clare, R. A.

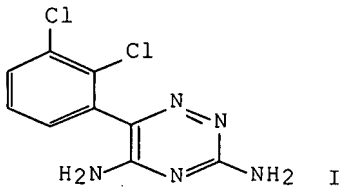
CORPORATE SOURCE: Dep. Bioanal. Sci., Wellcome Res. Lab., Beckenham/Kent, UK

SOURCE: Journal of Chromatography (1991), 554(1-2), 181-9
CODEN: JOCRAM; ISSN: 0021-9673

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB The use of thermospray liquid chromatog.-mass spectrometry allowed the structural elucidation of a number of urinary metabolites of Lamotrigine (I), formed after administering the drug to man, cynomolgus monkey, and rabbit. These data combined with the data obtained from high-performance liquid chromatog. with radiochem. detection, enabled the authors to determine the types amts. of unchanged drug and metabolites excreted in urine by man and a number of laboratory animal species. This technique was particularly useful as it highlighted a previously unknown fact that Lamotrigine is metabolized to

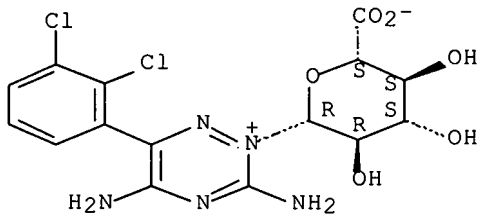
form 2 different N-glucuronides, one of which is resistant to cleavage in vitro by a crude β-glucuronidase preparation from Helix pomatia.

IT 135288-68-5 136565-76-9 136565-77-0
RL: ANT (Analyte); ANST (Analytical study)
(determination of, as Lamotrigine metabolite in urine by thermospray liquid chromatog.-mass spectrometry)

RN 135288-68-5 CAPLUS

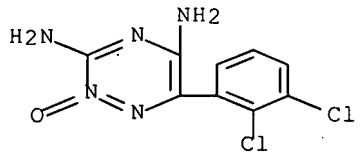
CN 1,2,4-Triazinium, 3,5-diamino-6-(2,3-dichlorophenyl)-2-β-D-glucopyranuronosyl-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 136565-76-9 CAPLUS

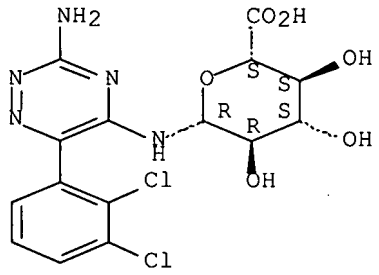
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)-, 2-oxide (9CI) (CA INDEX NAME)



RN 136565-77-0 CAPLUS

CN β-D-Glucopyranuronic acid, 1-[[3-amino-6-(2,3-dichlorophenyl)-1,2,4-triazin-5-yl]amino]-1-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



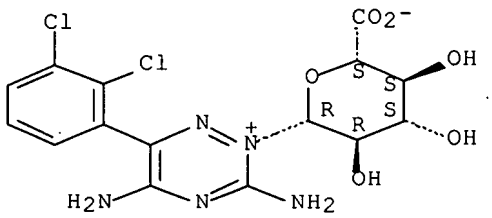
L21 ANSWER 46 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1991:463959 CAPLUS Full-text
DOCUMENT NUMBER: 115:63959
TITLE: A quaternary ammonium glucuronide is the major metabolite of lamotrigine in guinea pigs. In vitro and in vivo studies
AUTHOR(S): Remmel, Rory P.; Sinz, Michael W.
CORPORATE SOURCE: Coll. Pharm., Univ. Minnesota, Minneapolis, MN, 55455, USA
SOURCE: Drug Metabolism and Disposition (1991), 19(3), 630-6
CODEN: DMDSAI; ISSN: 0090-9556
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Urinary excretion of a variety of quaternary ammonium glucuronides has been generally reported to be confined to humans and some monkeys. Lower animal species appear to lack or have limited ability to form these unusual metabolites. In this report, the excretion of the quaternary ammonium glucuronide of lamotrigine, an investigational 1,2,4-triazine anticonvulsant, in guinea pigs is described. Lamotrigine 2-N-glucuronide accounted for 60% of an i.v. bolus dose of lamotrigine in guinea pig urine. Less than 6% of the dose was excreted unchanged. The pharmacokinetics of lamotrigine after an i.v. bolus dose of 10 mg/kg were determined with an ion-pairing, reversed-phase HPLC assay. Lamotrigine is a low-clearance drug (Cl = 2.51 mL/min/kg) with a large volume of distribution (Vas = 2.23 L/kg). The half-life of lamotrigine was 11.5 h. The elimination of the glucuronide was formation rate-limited and it was excreted by extensive tubular secretion. The glucuronide was also formed in Triton-X-100-activated liver microsomes and isolated guinea pig hepatocytes. The KM was 2.10 mM and the Vmax was 0.252 nmol/min/mg protein in untreated microsomes. Pretreatment with β-naphthoflavone did not induce lamotrigine glucuronidation. In hepatocytes, production of the glucuronide was linear for 60 min after a short lag period and 2 mM lamotrigine was not cytotoxic. Lamotrigine is only the second example of a compound that is primarily metabolized to a quaternary ammonium glucuronide in a lower animal species.

IT 135288-68-5
RL: BIOL (Biological study)
(as lamotrigine metabolite in guinea pig)
RN 135288-68-5 CAPLUS
CN 1,2,4-Triazinium, 3,5-diamino-6-(2,3-dichlorophenyl)-2-β-D-glucopyranuronosyl-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



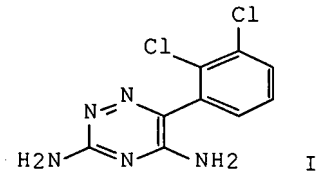
L21 ANSWER 47 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:177823 CAPLUS Full-text
DOCUMENT NUMBER: 114:177823
TITLE: Isolation and characterization of a novel quaternary

ammonium-linked glucuronide of lamotrigine

AUTHOR(S): Sinz, Michael W.; Remmel, Rory P.
CORPORATE SOURCE: Coll. Pharm., Univ. Minnesota, Minneapolis, MN, 55455, USA

SOURCE: Drug Metabolism and Disposition (1991), 19(1), 149-53
CODEN: DMDSAI; ISSN: 0090-9556
DOCUMENT TYPE: Journal
LANGUAGE: English

GI



I

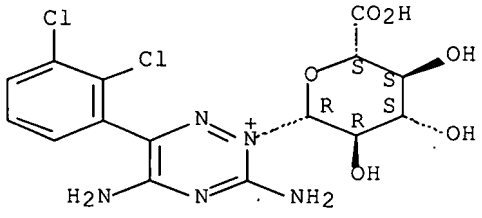
AB Lamotrigine (LTG, I) is a novel triazine anticonvulsant currently undergoing clin. trials. LTG N-glucuronide (II) the major human metabolite of I, was isolated from human urine by means of XAD-2 column chromatog. and semi-preparative HPLC. The structure of II was proven by mass spectroscopy and NMR spectroscopy, along with chemical and enzymic hydrolysis studies. High resolution fast atom bombardment mass spectrometry and electrospray tandem mass spectrometry of the glucuronide gave an M+ ion at 432.0 amu and a fragment ion at 256.0 (M - 176)+ amu. The proton NMR of the glucuronide indicated the presence of a glucuronic acid moiety. A downfield anomeric proton (5.35-5.60 ppm) implied direct attachment to the aromatic triazine ring. Carbon-13 NMR of II revealed an upfield shift (Δ = -7.0 ppm) of the C-3 carbon of the triazine ring compared to I, indicating attachment of the glucuronide to the N-2 position. Chemical degradation or rearrangement of II occurs at neutral pH to produce an unknown product (RP-1), while at basic pH a different unknown product (RP-2) is formed. II is unusually stable at acidic pH. Treatment of II with β-glucuronidase resulted in hydrolysis to I, and enzymic hydrolysis was inhibited by saccharo-1,4-lactone.

IT 133310-19-7
RL: BIOL (Biological study)
(isolation and structure of, as lamotrigine metabolite in human urine)

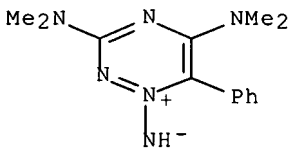
RN 133310-19-7 CAPLUS

CN 1,2,4-Triazinium, 3,5-diamino-6-(2,3-dichlorophenyl)-2-β-D-glucopyranuronosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L21 ANSWER 48 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:601865 CAPLUS Full-text
DOCUMENT NUMBER: 113:201865
TITLE: Structure of 3,5-bis(dimethylamino)-6-phenyl-1,2,4-triazine 1-imide
AUTHOR(S): Lindley, Peter F.; Boyd, Gerhard V.; Nicolaou, George A.
CORPORATE SOURCE: Dep. Crystallogr., Birkbeck Coll., London, WC1E 7HX, UK
SOURCE: Acta Crystallographica, Section C: Crystal Structure Communications (1990), C46(8), 1487-90
CODEN: ACSCEE; ISSN: 0108-2701
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The title compound is orthorhombic, space group P21212, with a 15.095(3), b 16.333(3), and c 5.643(1) Å; dc = 1.233 for Z = 4. The final R = 0.042 and Rw = 0.046 for 2500 reflections. Atomic coordinates are given. The triazide ring is not strictly planar, the Ph ring makes an angle of -63.5° with the plane through N1,N2,C5,N11. The bond distances in the triazinium imide, particularly the N1-N11(imide) at 1.296 Å, indicate that canonical forms involving an exocyclic N-N double bond at N1 make important contributions to the overall resonance hybrid. The structure contains intermol. H bonds involving the imide H atom.
IT 101960-44-5
RL: PRP (Properties)
(crystal structure of)
RN 101960-44-5 CAPLUS
CN 1,2,4-Triazinium, 1-amino-3,5-bis(dimethylamino)-6-phenyl-, inner salt (9CI) (CA INDEX NAME)



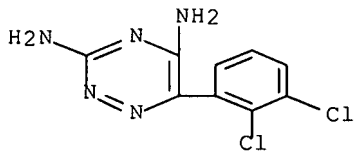
L21 ANSWER 49 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:126056 CAPLUS Full-text
DOCUMENT NUMBER: 110:126056
TITLE: Structure of lamotrigine methanol solvate: 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine-methanol, a novel anticonvulsant drug
AUTHOR(S): Janes, Robert W.; Lisgarten, John N.; Palmer, Rex A.
CORPORATE SOURCE: Birkbeck Coll., Univ. London, London, WC1E 7HX, UK
SOURCE: Acta Crystallographica, Section C: Crystal Structure Communications (1989), C45(1), 129-32
CODEN: ACSCEE; ISSN: 0108-2701
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The title compound is monoclinic, space group P21/n, with a 15.456(3), b 11.736(2), c 7.300(3) Å, and β 94.417(3)°; Z = 4 for dc = 1.449. The final R = 0.055 for 2444 reflections. Atomic coordinates are given. The Ph and

triazine aromatic rings make a dihedral angle of 80.6(9)° with each other. The bond linking the 2 rings is 1.480(3) Å. The structure is stabilized by a network of H bonds involving amino and ring N atoms, one of the Cl atoms, and the MeOH of crystallization

IT 119441-74-6
RL: PRP (Properties)
(crystal structure of)
RN 119441-74-6 CAPLUS
CN Methanol, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (1:1) (9CI) (CA INDEX NAME)

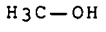
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

CRN 67-56-1
CMF C H4 O



L21 ANSWER 50 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:112505 CAPLUS Full-text
DOCUMENT NUMBER: 108:112505
TITLE: Preparation of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine isethionate as an antiepileptic
INVENTOR(S): Sawyer, David Alan; Copp, Frederick Charles
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Eur. Pat. Appl., 5 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 247892	A1	19871202	EP 1987-304776	19870529 <--
EP 247892	B1	19910424		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DK 8702759	A	19871201	DK 1987-2759	19870529 <--

DK 166278	B	19930329			
DK 166278	C	19930823			
FI 8702406	A	19871201	FI 1987-2406	19870529	<--
FI 90770	B	19931215			
FI 90770	C	19940325			
AU 8773684	A	19871203	AU 1987-73684	19870529	<--
AU 597982	B2	19900614			
JP 62289570	A	19871216	JP 1987-134772	19870529	<--
JP 07051571	B	19950605			
HU 45978	A2	19880928	HU 1987-2487	19870529	<--
HU 196769	B	19890130			
ZA 8703896	A	19890125	ZA 1987-3896	19870529	<--
US 4847249	A	19890711	US 1987-56136	19870529	<--
AT 62902	T	19910515	AT 1987-304776	19870529	<--
CA 1286670	C	19910723	CA 1987-538395	19870529	<--
IL 82710	A	19920115	IL 1987-82710	19870529	<--
PRIORITY APPLN. INFO.:			GB 1986-13183	A 19860530	<--
			EP 1987-304776	A 19870529	<--

AB The title compound (I.isethionate), useful as an anticonvulsant (no data), was prepared by reaction of I with 2-hydroxyethanesulfonic acid (II) or by reaction of I salts with the anion of II. A 1.0 M solution of Na isethionate in H2O was passed through a column of IR 120 (H) ion exchange resin. I (preparation given) was added to the resulting II and the solution was filtered and evaporated Recrystn. from industrial methylated spirit gave 72% I.isethionate.

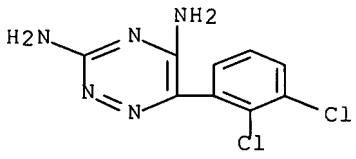
IT 113170-86-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as anticonvulsant)

RN 113170-86-8 CAPLUS

CN Ethanesulfonic acid, 2-hydroxy-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (1:1) (9CI) (CA INDEX NAME)

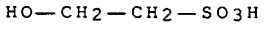
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

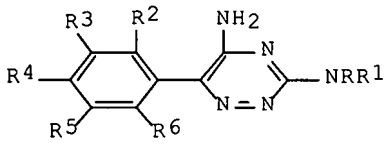
CRN 107-36-8
CMF C2 H6 O4 S



L21 ANSWER 51 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:200211 CAPLUS Full-text
DOCUMENT NUMBER: 104:200211
TITLE: 1,2,4-Triazines for treating gastrointestinal motility dysfunction
INVENTOR(S): Kuhla, Donald E.; Studt, William L.; Campbell, Henry F.; Yelnosky, John
PATENT ASSIGNEE(S): William H. Rorer, Inc., USA
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4563456	A	19860107	US 1984-570547	19840113 <--
PRIORITY APPLN. INFO.:			US 1984-570547	19840113 <--

OTHER SOURCE(S): MARPAT 104:200211
GI

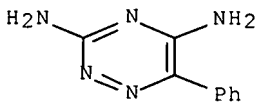


I

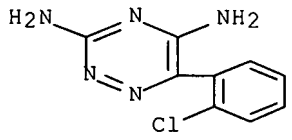
AB 3,5-Diamino-6-(substituted phenyl)-1,2,4-triazines (I, R, R1 = H, alkyl, alkenyl, heterocyclic, cycloalkyl, etc.; NRR1 = 5-7-membered ring optionally substituted with 0-1 N, O S; R2-R6 = H, halo, alkyl, nitro, amino, hydroxy, etc.) and their salts and pharmaceutical formulations are described for possible treatment of gastrointestinal motility dysfunctions, especially irritable bowel syndrome. The test compds. exhibited therapeutic effectiveness in various exptl. gastrointestinal motility disorders in laboratory animals.

IT 6719-24-0D, derivs. 38943-73-6 38943-76-9
RL: BIOL (Biological study)
(irritable bowel syndrome treatment with)

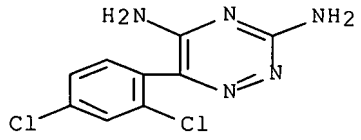
RN 6719-24-0 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-phenyl- (9CI) (CA INDEX NAME)



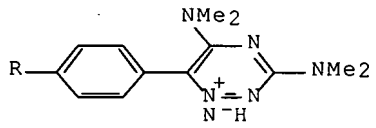
RN 38943-73-6 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2-chlorophenyl)- (9CI) (CA INDEX NAME)



RN 38943-76-9 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,4-dichlorophenyl)- (9CI) (CA INDEX NAME)



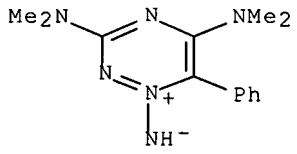
L21 ANSWER 52 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:186381 CAPLUS Full-text
DOCUMENT NUMBER: 104:186381
TITLE: Formation of 1,2,4-triazinium 1-imides from 4-aryl-1-azido-1,3-bis(dimethylamino)-2-azabutenylium salts: heterocyclic N-imides lacking exocyclic stabilization
AUTHOR(S): Boyd, Gerhard V.; Lindley, Peter F.; Mitchell, John C.; Nicolaou, George A.
CORPORATE SOURCE: Dep. Chem., Queen Elizabeth Coll., London, W8 7AH, UK
SOURCE: Journal of the Chemical Society, Chemical Communications (1985), (21), 1522-3
CODEN: JCCCAT; ISSN: 0022-4936
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 104:186381
GI



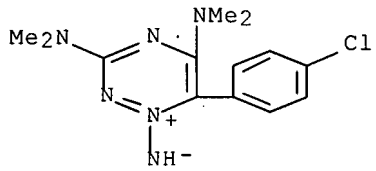
I

AB The triazinium imides I [R = H (II), Me, MeO, Cl] were prepared in 34-90% yield by cyclization of the appropriate 4-RC6H4CH2C(NMe2):NCN3:N+Me2 ClO4- on treatment with NaOH. The structure of II was determined by x-ray crystallog.
IT 101960-44-5P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and mol. and crystal structure of)
RN 101960-44-5 CAPLUS
CN 1,2,4-Triazinium, 1-amino-3,5-bis(dimethylamino)-6-phenyl-, inner salt (9CI) (CA INDEX NAME)



IT 101960-47-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 101960-47-8 CAPLUS
CN 1,2,4-Triazinium, 1-amino-6-(4-chlorophenyl)-3,5-bis(dimethylamino)-, inner salt (9CI) (CA INDEX NAME)

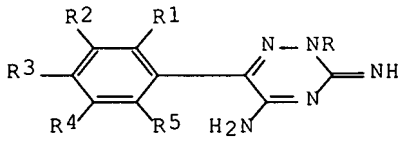


L21 ANSWER 53 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1985:542021 CAPLUS Full-text
DOCUMENT NUMBER: 103:142021
TITLE: Triazine compounds having cardiovascular activity
INVENTOR(S): Allan, Geoffrey; Miller, Alastair Ainslie; Sawyer, David Alan
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 142306	A2	19850522	EP 1984-307374	19841026 <--
EP 142306	A3	19861120		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4649139	A	19870310	US 1984-663682	19841022 <--
DK 8405121	A	19850428	DK 1984-5121	19841026 <--
FI 8404212	A	19850428	FI 1984-4212	19841026 <--
AU 8434758	A	19850509	AU 1984-34758	19841026 <--
AU 564667	B2	19870820		

JP 60109577	A	19850615	JP 1984-225636		19841026 <--
DD 224033	A5	19850626	DD 1984-268757		19841026 <--
HU 36102	A2	19850828	HU 1984-4003		19841026 <--
HU 191566	B	19870330			
ES 537104	A1	19860416	ES 1984-537104		19841026 <--
ZA 8408388	A	19860625	ZA 1984-8388		19841026 <--
SU 1371500	A3	19880130	SU 1984-3805251		19841026 <--
IL 73332	A	19880630	IL 1984-73332		19841026 <--
PL 144899	B1	19880730	PL 1984-250213		19841026 <--
CA 1261328	A1	19890926	CA 1984-466473		19841026 <--
PRIORITY APPLN. INFO.:			GB 1983-28757	A	19831027 <--
OTHER SOURCE(S):	MARPAT 103:142021				

GI



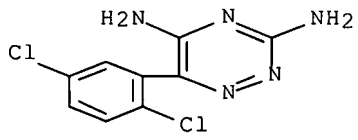
I

AB Tautomeric iminotriazinamines I [R = (un)substituted C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, C3-10 cycloalkyl; R1-R5 = H, halogen, alkenyloxy, acyl, acyloxy, cyano, NO2, aryl, alkylthio, (un)substituted alkyl, alkenyl, alkynyl, alkoxy, amino; R1R2, R2R3, R3R4, R4R5 = CH:CHCH:CH] were prepared Thus, 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine was alkylated with Me2CHI to give I-HI (R = Me2CH, R1 = R2 = Cl; R3-R5 = H) which was converted to the mesylate salt (II) (12% overall yield). II at 1 mg/kg i.v. to rats increased the amount of aconitine required to elicit ventricular arrhythmias by 490% compared with 84% for 1 mg/kg verapamil.

IT 77668-43-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-methylation of)

RN 77668-43-0 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(2,5-dichlorophenyl)- (9CI) (CA INDEX NAME)



L21 ANSWER 54 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1983:89397 CAPLUS Full-text
DOCUMENT NUMBER:	98:89397
TITLE:	Substituted aromatic compounds
INVENTOR(S):	Baxter, Martin G.; Elphick, Albert R.; Miller, Alistair A.; Sawyer, David A.
PATENT ASSIGNEE(S):	Wellcome Foundation Ltd., UK
SOURCE:	Can., 26 pp. Division of Can. Appl. No. 353,081.

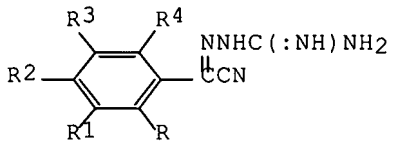
CODEN: CAXXA4
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 1133938	A2	19821019	CA 1981-373126	19810316 <--
CA 1112643	A1	19811117	CA 1980-353081	19800530 <--
US 4486354	A	19841204	US 1981-308805	19811005 <--
AU 566870	B2	19871105	AU 1983-14051	19830428 <--
US 4602017	A	19860722	US 1984-583286	19840227 <--
FI 8400888	A	19840306	FI 1984-888	19840306 <--
FI 73203	B	19870529		
FI 73203	C	19870910		

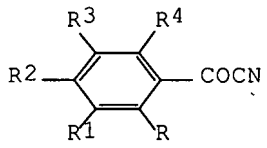
PRIORITY APPLN. INFO.:

GB 1979-19257	A	19790601 <--
CA 1980-353081	A3	19800530 <--
US 1980-154198	A1	19800529 <--
FI 1980-1758	A	19800530 <--
CA 1981-373126		19810316 <--
US 1981-302365	A1	19810915 <--

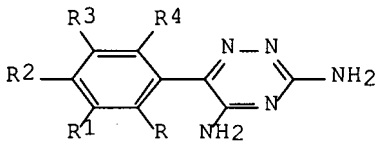
GI



I



II



III

AB [(Cyanobenzylidene)amino]guanidines I (R-R4 = H, halo, alkyl, F3C; RR1 = HC:CHCH:CH, halobenzo, trifluoromethylbenzo, alkylbenzo) were prepared from the benzoyl cyanides II and H2NNHC(:NH)NH2 and were useful as intermediates in the preparation of anticonvulsant triazines III. Thus, 2,3-Cl2C6H3COCl was treated with CuCN to give 2,3-Cl2C6H3COCN which was treated with H2NNHC(:NH)NH2 to give I (R = R1 = Cl, R2 = R3 = R4 = H), which was cyclized by KOH to give III (R = R2 = Cl, R2 = R3 = R4 = H) (IV). The anticonvulsant ED50 of IV was 2.4 mg/kg in the maximal electroshock test.

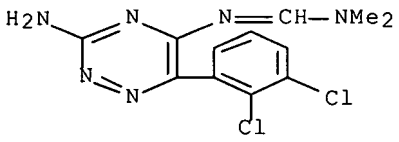
IT 77668-59-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticonvulsant activity of)

RN 77668-59-8 CAPLUS

CN Methanimidamide, N'-[3-amino-6-(2,3-dichlorophenyl)-1,2,4-triazin-5-yl]-N,N-dimethyl-, ethanedioate (9CI) (CA INDEX NAME)

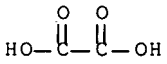
CM 1

CRN 77668-58-7
CMF C12 H12 Cl2 N6

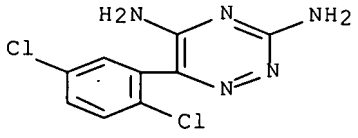


CM 2

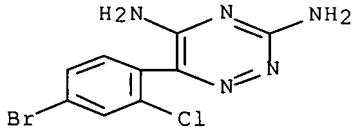
CRN 144-62-7
CMF C2 H2 O4



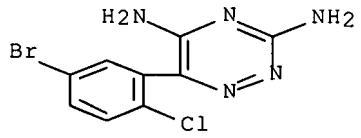
IT 77668-43-0P 77668-44-1P 77668-45-2P
77668-46-3P 77668-47-4P 77668-49-6P
77668-50-9P 77668-51-0P 77668-56-5P
77668-57-6P 77668-58-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and anticonvulsant activity of)
RN 77668-43-0 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,5-dichlorophenyl)- (9CI) (CA INDEX NAME)



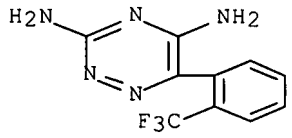
RN 77668-44-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(4-bromo-2-chlorophenyl)- (9CI) (CA INDEX NAME)



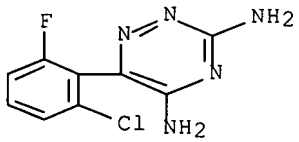
RN 77668-45-2 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(5-bromo-2-chlorophenyl)- (9CI) (CA INDEX NAME)



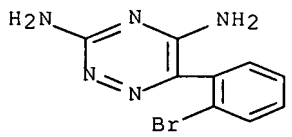
RN 77668-46-3 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 77668-47-4 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2-chloro-6-fluorophenyl)- (9CI) (CA INDEX NAME)

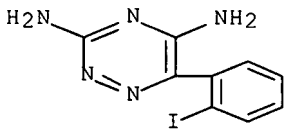


RN 77668-49-6 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2-bromophenyl)- (9CI) (CA INDEX NAME)

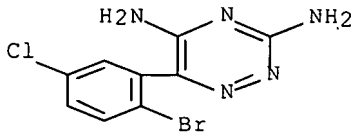


RN 77668-50-9 CAPLUS

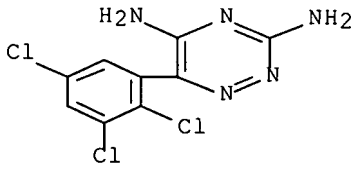
CN 1,2,4-Triazine-3,5-diamine, 6-(2-iodophenyl)- (9CI) (CA INDEX NAME)



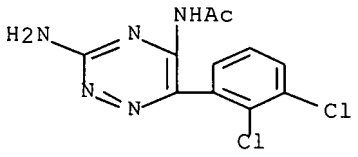
RN 77668-51-0 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2-bromo-5-chlorophenyl)- (9CI) (CA INDEX NAME)



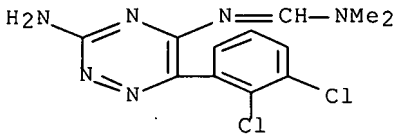
RN 77668-56-5 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3,5-trichlorophenyl)- (9CI) (CA INDEX NAME)



RN 77668-57-6 CAPLUS
CN Acetamide, N-[3-amino-6-(2,3-dichlorophenyl)-1,2,4-triazin-5-yl]- (9CI) (CA INDEX NAME)



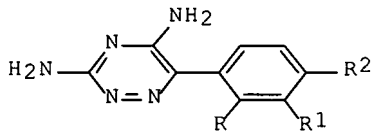
RN 77668-58-7 CAPLUS
CN Methanimidamide, N'-[3-amino-6-(2,3-dichlorophenyl)-1,2,4-triazin-5-yl]-N,N-dimethyl- (9CI) (CA INDEX NAME)



L21 ANSWER 55 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:430402 CAPLUS Full-text
DOCUMENT NUMBER: 95:30402
TITLE: Substituted aryl triazine compounds and pharmaceutical compositions containing them
INVENTOR(S): Roth, Barbara; Miller, Alistair Ainslie; Sawyer, David Alan
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 24351	A1	19810304	EP 1980-104841	19800814 <--
EP 24351	B1	19841031		
R: BE, CH, DE, FR, GB, NL, SE				
US 4311701	A	19820119	US 1980-177886	19800814 <--
EP 86502	A2	19830824	EP 1983-102429	19800814 <--
EP 86502	A3	19840201		
EP 86502	B1	19870325		
R: BE, CH, DE, FR, GB, LI, NL, SE				
JP 56030921	A	19810328	JP 1980-112608	19800815 <--
JP 02006739	B	19900213		

PRIORITY APPLN. INFO.: GB 1979-28641 A 19790816 <--
EP 1980-104841 A 19800814 <--
OTHER SOURCE(S): MARPAT 95:30402
GI



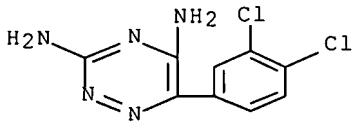
I

AB Oral pharmaceutical compns. containing substituted triazines (I, R-R2 = H or Cl) and their salts are used for the treatment of central nervous system disorders such as epilepsy. A mixture of 3,5-diamino-6-(2,4-dichlorophenyl)-1,2,4-triazine (I, R = R2 = O, R1 = H) (II) [38943-76-9] 150, lactose 200,

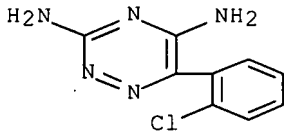
maize starch 50, poly(vinylpyrrolidone) 4, and Mg stearate 4 mg gave a tablet of average weight 408 mg. The dose range for adult humans for the treatment of epilepsy was from 20 to 2400 mg/day. The ED50 in mice for II was 18.7 mg/kg oral.

IT 36518-85-1 38943-73-6 38943-76-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals containing, for epilepsy treatment)

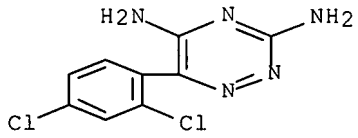
RN 36518-85-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(3,4-dichlorophenyl)- (9CI) (CA INDEX NAME)



RN 38943-73-6 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2-chlorophenyl)- (9CI) (CA INDEX NAME)



RN 38943-76-9 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,4-dichlorophenyl)- (9CI) (CA INDEX NAME)



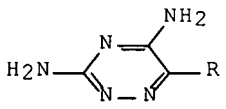
L21 ANSWER 56 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1981:208915 CAPLUS Full-text
DOCUMENT NUMBER:	94:208915
TITLE:	3,5-Diamino-1,2,4-triazine derivatives pharmaceutical compositions and intermediates
INVENTOR(S):	Baxter, Martin George; Elphick, Albert Reginald; Miller, Alistair Ainslie; Sawyer, David Alan
PATENT ASSIGNEE(S):	Wellcome Foundation Ltd., UK
SOURCE:	Eur. Pat. Appl., 14 pp. CODEN: EPXXDW
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 21120	A1	19810107	EP 1980-103031	19800530 <--
EP 21120	B1	19830406		
R: CH, DE, FR, GB, IT				
JP 56025170	A	19810310	JP 1980-71581	19800530 <--
JP 02006751	B	19900213		
US 4560687	A	19851224	US 1984-585022	19840305 <--
PRIORITY APPLN. INFO.:			GB 1979-19256 A	19790601 <--
			US 1980-154199 A3	19800529 <--
			US 1981-302407 A1	19810915 <--

GI



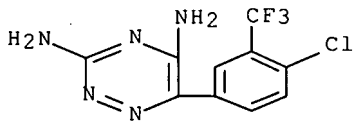
I

AB Triazinediamines I (R = optionally substituted Ph, naphthyl) were prepared Thus, 4,3-Cl(CF3)C6H3CO2H was converted to the chloride and treated with CuCN to give 4,3-Cl(CF3)C6H3COCN which was cyclized with H2NNHC(:NH)NH2.H2CO3 to give I [R = 4,3-Cl(CF3)C6H3]. The latter compound had an anticonvulsant ED50 of 18.5 mg/kg orally in mice.

IT 77668-39-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and anticonvulsant activity of)

RN 77668-39-4 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-[4-chloro-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



L21 ANSWER 57 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1981:208914 CAPLUS Full-text

DOCUMENT NUMBER: 94:208914

TITLE: 1,2,4-Triazine derivatives, pharmaceutical compositions and intermediates utilized for their preparation

INVENTOR(S): Baxter, Martin George; Elphick, Albert Reginald; Miller, Alistair Ainslie; Sawyer, David Alan

PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK

SOURCE: Eur. Pat. Appl., 22 pp.

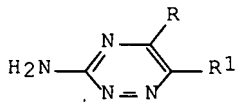
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 21121	A1	19810107	EP 1980-103032	19800530 <--
EP 21121	B1	19830511		
R: BE, CH, DE, FR, GB, LU, NL, SE				
DK 8002338	A	19801202	DK 1980-2338	19800530 <--
DK 153787	B	19880905		
DK 153787	C	19890116		
FI 8001758	A	19801202	FI 1980-1758	19800530 <--
FI 67844	B	19850228		
FI 67844	C	19850610		
AU 8058906	A	19801204	AU 1980-58906	19800530 <--
AU 530999	B2	19830804		
JP 56025169	A	19810310	JP 1980-71580	19800530 <--
JP 01044706	B	19890929		
ES 491998	A1	19810516	ES 1980-491998	19800530 <--
DD 151309	A5	19811014	DD 1980-221474	19800530 <--
ZA 8003250	A	19820127	ZA 1980-3250	19800530 <--
AT 8002896	A	19820715	AT 1980-2896	19800530 <--
AT 370097	B	19830225		
EP 59987	A1	19820915	EP 1982-102293	19800530 <--
EP 59987	B1	19850814		
R: BE, CH, DE, FR, GB, LU, NL, SE				
PL 124029	B1	19821231	PL 1980-224633	19800530 <--
HU 24621	A2	19830328	HU 1980-1364	19800530 <--
HU 182086	B	19831228		
IL 60201	A	19840531	IL 1980-60201	19800530 <--
CS 234018	B2	19850314	CS 1980-3829	19800530 <--
SU 1055331	A3	19831115	SU 1980-2932704	19800602 <--
US 4486354	A	19841204	US 1981-308805	19811005 <--
US 4602017	A	19860722	US 1984-583286	19840227 <--
FI 8400888	A	19840306	FI 1984-888	19840306 <--
FI 73203	B	19870529		
FI 73203	C	19870910		
JP 61033163	A	19860217	JP 1985-121370	19850604 <--
JP 01044179	B	19890926		

PRIORITY APPLN. INFO.:

GB 1979-19257	A	19790601 <--
US 1980-154198	A1	19800529 <--
EP 1980-103032	A	19800530 <--
FI 1980-1758	A	19800530 <--
US 1981-302365	A1	19810915 <--

OTHER SOURCE(S): MARPAT 94:208914
GI

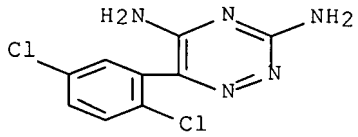


I

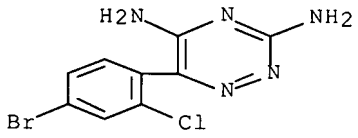
AB Triazines I (R = NH2, acylamino, aminomethyleneamino; R1 = substituted Ph) were prepared Thus, 2,3-Cl2C6H3I was Grignard carboxlated and the 2,3-Cl2C6H3CO2H converted to the chloride and treated with CuCN to give 2,3-Cl2C6H3COCN which was cyclized with aminoguanidine bicarbonate to I (R = NH2, R1 = 2,3-Cl2C6H3). The latter compound had an anticonvulsant ED50 of 2.4 mg/kg orally in mice.

IT 77668-43-0P 77668-44-1P 77668-45-2P
77668-46-3P 77668-47-4P 77668-49-6P
77668-50-9P 77668-51-0P 77668-56-5P
77668-57-6P 77668-59-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and anticonvulsant activity of)

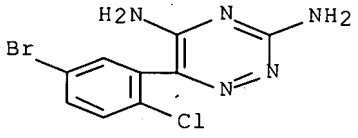
RN 77668-43-0 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,5-dichlorophenyl)- (9CI) (CA INDEX NAME)



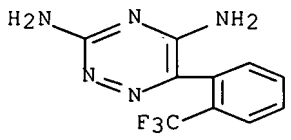
RN 77668-44-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(4-bromo-2-chlorophenyl)- (9CI) (CA INDEX NAME)



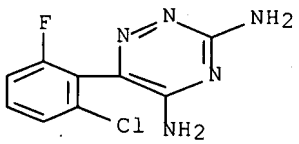
RN 77668-45-2 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(5-bromo-2-chlorophenyl)- (9CI) (CA INDEX NAME)



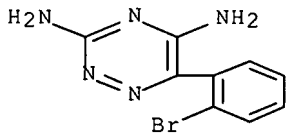
RN 77668-46-3 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



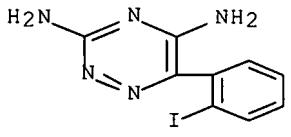
RN 77668-47-4 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2-chloro-6-fluorophenyl)- (9CI) (CA INDEX NAME)



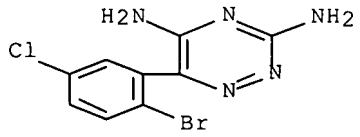
RN 77668-49-6 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2-bromophenyl)- (9CI) (CA INDEX NAME)



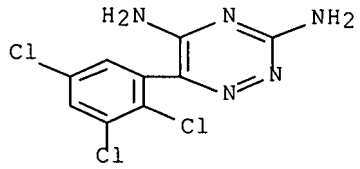
RN 77668-50-9 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2-iodophenyl)- (9CI) (CA INDEX NAME)



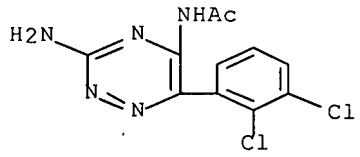
RN 77668-51-0 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2-bromo-5-chlorophenyl)- (9CI) (CA INDEX NAME)



RN 77668-56-5 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3,5-trichlorophenyl)- (9CI) (CA INDEX NAME)



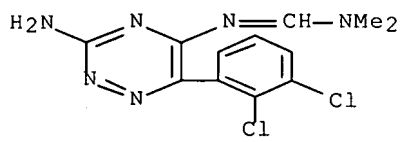
RN 77668-57-6 CAPLUS
CN Acetamide, N-[3-amino-6-(2,3-dichlorophenyl)-1,2,4-triazin-5-yl]- (9CI) (CA INDEX NAME)



RN 77668-59-8 CAPLUS
CN Methanimidamide, N'-[3-amino-6-(2,3-dichlorophenyl)-1,2,4-triazin-5-yl]-N,N-dimethyl-, ethanedioate (9CI) (CA INDEX NAME)

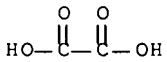
CM 1

CRN 77668-58-7
CMF C12 H12 Cl2 N6



CM 2

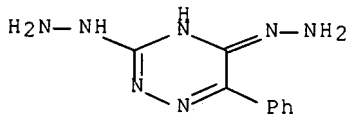
CRN 144-62-7
CMF C2 H2 O4



L21 ANSWER 58 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1979:473892 CAPLUS Full-text
DOCUMENT NUMBER: 91:73892
TITLE: Studies on the chemistry of pharmacologically active heterocycles. Part I. Acid hydrolysis of hydrazino-1,2,4-triazine derivatives
AUTHOR(S): Daneshtalab, M.; Khalaj, A.; Lalezari, I.
CORPORATE SOURCE: Coll. Pharm., Univ. Tehran, Teheran, Iran
SOURCE: Journal of Heterocyclic Chemistry (1979), 16(4), 817-19
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 91:73892

AB The acid hydrolysis of 3-hydrazino-5,6-disubstituted-1,2,4-triazine, 3,5-dihydrazino-6-substituted-1,2,4-triazine, and 2-hydrazinopyrimidine derivs. was studied. The reaction proceeded through the formation of 3-keto and 3,5-diketo derivs. of the related 2,3-dihydro, 2,3,4,5-tetrahydro-1,2,4-triazines, and 2-keto derivs. of 1,2-dihydropyrimidines. In 1,2,4-triazine derivs. the C-5 carbon is more reactive than the C-3 carbon toward nucleophiles. The reaction mechanism is discussed.

IT 70997-61-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(acid catalyzed hydrolysis of, kinetics of)
RN 70997-61-4 CAPLUS
CN 1,2,4-Triazine-3,5(2H,4H)-dione, 6-phenyl-, dihydrazone (9CI) (CA INDEX NAME)



L21 ANSWER 59 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1977:512003 CAPLUS Full-text
DOCUMENT NUMBER: 87:112003
TITLE: Method of viral chemoprophylaxis
INVENTOR(S): Hegarty, Charles Paul; Pietryk, Helen C.
PATENT ASSIGNEE(S): American Home Products Corp., USA
SOURCE: U.S., 27 pp.
CODEN: USXXAM

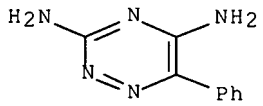
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4032659	A	19770628	US 1975-590536	19750626 <--
PRIORITY APPLN. INFO.:			US 1969-808989 A3	19690320 <--

AB Compds. possessing a stereochem. unencumbered nitrogen-nitrogen bond exhibited antiviral activity, at very low doses. Thus, hydrazine sulfate [10034-93-2], hydrazine derivs., and related compds. had chemoprophylactic effects in mice infected with both DNA and RNA viruses at levels of infection that killed 100% of the control animals. Best results were obtained when drugs were administered orally, prior to infection, and in several doses at 48-h intervals. The degree of protection was most extensive at low virus challenges, a situation frequently encountered in many viral diseases of higher animals.

IT 6719-24-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiviral activity of)

RN 6719-24-0 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-phenyl- (9CI) (CA INDEX NAME)



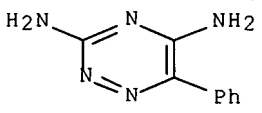
L21 ANSWER 60 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1977:433694 CAPLUS Full-text
DOCUMENT NUMBER: 87:33694
TITLE: Viral chemoprophylaxis
INVENTOR(S): Hegarty, Charles Paul; Pietryk, Helen C.
PATENT ASSIGNEE(S): American Home Products Corp., USA
SOURCE: U.S., 27 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4027039	A	19770531	US 1975-590543	19750626 <--
PRIORITY APPLN. INFO.:			US 1969-808989 A3	19690320 <--

AB By oral administration of .apprx.25 kg to 250 μg/kg, H2NNH2, its derivs., and related compds. protect animals against diseases caused by DNA and RNA viruses. Thus, thiosemicarbazide [79-19-6] was active against influenza virus Ann Arbor and PR 8, vaccinia virus, Mengo virus, and herpes virus in mice and against vaccinia virus in rabbits.

IT 6719-24-0

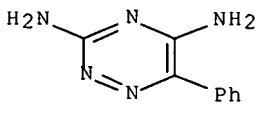
RL: BIOL (Biological study)
(virus inhibition by)
RN 6719-24-0 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-phenyl- (9CI) (CA INDEX NAME)



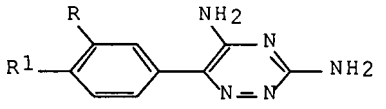
L21 ANSWER 61 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1976:554151 CAPLUS Full-text
DOCUMENT NUMBER: 85:154151
TITLE: Compounds for viral chemoprophylaxis
INVENTOR(S): Hegarty, Charles P.; Pietryk, Helen C.
PATENT ASSIGNEE(S): American Home Products Corp., USA
SOURCE: U.S., 29 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3980774	A	19760914	US 1974-530888	19741209 <--
PRIORITY APPLN. INFO.:			US 1969-808989 A3	19690320 <--

AB Hydrazine [302-01-2], hydrazine derivs., and its related compds. were active in protecting animals against disease caused by both DNA and RNA type viruses at doses of about 250 pg to 250 μg/kg. Compds. which afforded unencumbered access to a nitrogen-nitrogen bond were active. The acute toxicity of the more toxic compds. was about 25 mg/kg, and therefore the effective dose was less than 1/1000 of the acute toxic dose. Optimal efficacy was dependent upon the dose-dose schedule relationship, appearing to be more active when the drug was administered at 48 hr intervals, with prolonged pre-treatment. All of the compds. tested were as effective, or more effective after oral administration than they were after parenteral administration.
IT 6719-24-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiviral activity of)
RN 6719-24-0 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-phenyl- (9CI) (CA INDEX NAME)



L21 ANSWER 62 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1976:400180 CAPLUS Full-text
DOCUMENT NUMBER: 85:180
TITLE: Antimalarials. 3. 1,2,4-Triazines
AUTHOR(S): March, Louis C.; Bajwa, Gurdip S.; Lee, Jessie; Wasti, Khizar; Joullie, Madeleine M.
CORPORATE SOURCE: Dep. Chem., Univ. Pennsylvania, Philadelphia, PA, USA
SOURCE: Journal of Medicinal Chemistry (1976), 19(6), 845-8
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

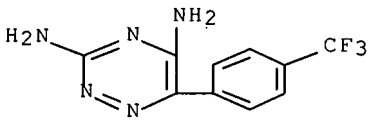


I, R=H, R1=CF_3
II, RR1=OCH_2O

AB The syntheses of 39 title compds. as potential antimalarials are described. The structural requirements for antimalarial activity are discussed with reference to the substituents of a phenyl group in the 6 position and amino groups at the 3 and 5 positions. Of the compds. tested, 3,5-diamino-6-(4-trifluoromethylphenyl)-1,2,4-triazine (I) [35857-39-7], 3,5-diamino-6-(3,4-methylenedioxyphenyl)-1,2,4- triazine (II) [58848-65-0] and 3,5-diamino-6-(3-chloro-4-methylphenyl)- 1,2,4-triazine [58848-67-2] produced cures in mice infected with Plasmodium berghei. I, II, 3,5-diamino-6-(m-trifluoromethylphenyl)-1,2,4- triazine [35857-40-0], 3,5-diamino-6-(p-methylsulfonylphenyl)- 1,2,4-triazine [58848-68-3], 3,5-bis[[(dimethylamino)methylene]amino]-6- (3,4-methylenedioxyphenyl)-1,2,4-triazine [58848-72-9], and 3,5-bis(methylthio)-6-methyl-1,2,4-triazizne [7448-21-7] produced cures in chicks infected with P. gallinaceum.

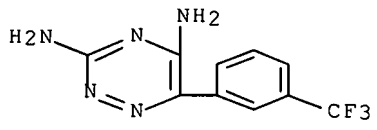
IT 35857-39-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimalarial activity of)

RN 35857-39-7 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

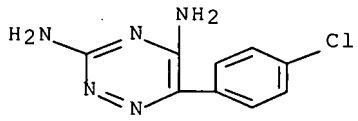


IT 35857-40-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

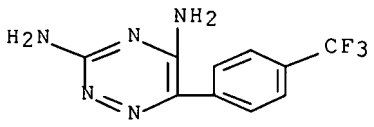
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antimalarial activity of)
RN 35857-40-0 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



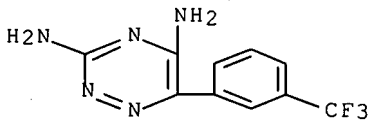
L21 ANSWER 63 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1972:522123 CAPLUS Full-text
DOCUMENT NUMBER: 77:122123
TITLE: Antimalarial activities of some 3,5-diamino-as-triazine derivatives
AUTHOR(S): Rees, Richard W. A.; Russell, Peter B.; Foell, Theodore J.; Bright, Royal E.
CORPORATE SOURCE: Res. Div., Wyeth Lab., Inc., Radnor, PA, USA
SOURCE: Journal of Medicinal Chemistry (1972), 15(8), 859-61
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 3,5-Diamino-6-(3,4-dichlorophenyl)-as-triazine [36518-85-1], the most potent of a series of as-triazines tested against Plasmodium berghei in mice, was also the most toxic (maximum tolerated dose 40 mg/kg; min. curative dose 5 mg/kg). However, 3,5-diamino-6-(α,α,α- trifluoro-p-tolyl)-as-triazine (I) [35857-39-7] combined high activity (min. curative dose 10 mg/kg) with relatively low toxicity (maximum tolerated dose >640 mg/kg). I was suppressive against cycloguanil-resistant P. berghei in mice, curative against P. cynomolgi in rhesus monkeys, and suppressive against P. falciparum in owl monkeys (Aotus trivirgatus). To synthesize I, (α,α,α-trifluoro- p-tolyl)glyoxylonitrile, prepared by the action of CuCN on the corresponding aroyl halide, was reacted with aminoguanidine in strongly acidic solution, and the resulting amidinohydrazone was refluxed in KOH-EtOH under N2 to effect ring closure.
IT 6662-28-8 35857-39-7 35857-40-0
35857-41-1 35857-42-2 36518-85-1
38943-73-6 38943-74-7 38943-76-9
38943-80-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimalarial activity of)
RN 6662-28-8 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(4-chlorophenyl)- (9CI) (CA INDEX NAME)



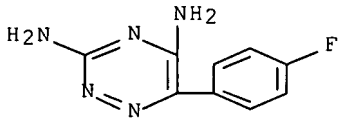
RN 35857-39-7 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



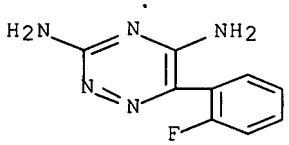
RN 35857-40-0 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



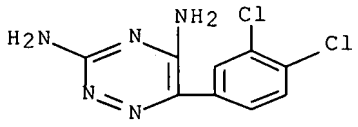
RN 35857-41-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



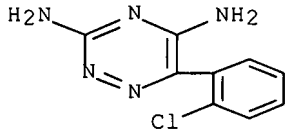
RN 35857-42-2 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



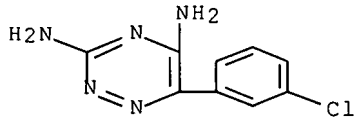
RN 36518-85-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(3,4-dichlorophenyl)- (9CI) (CA INDEX NAME)



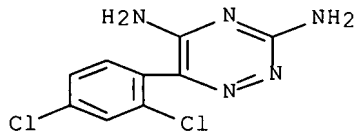
RN 38943-73-6 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2-chlorophenyl)- (9CI) (CA INDEX NAME)



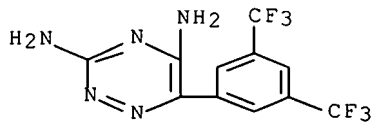
RN 38943-74-7 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(3-chlorophenyl)- (9CI) (CA INDEX NAME)



RN 38943-76-9 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,4-dichlorophenyl)- (9CI) (CA INDEX NAME)



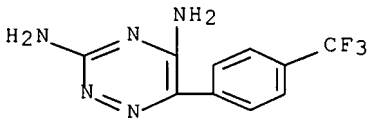
RN 38943-80-5 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-[3,5-bis(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



IT 38917-85-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 38917-85-0 CAPLUS
CN 2-Naphthalenecarboxylic acid, 4,4'-methylenebis[3-hydroxy-, compd. with 6-[4-(trifluoromethyl)phenyl]-1,2,4-triazine-3,5-diamine (1:2) (9CI) (CA INDEX NAME)

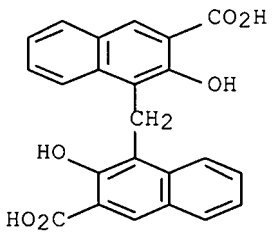
CM 1

CRN 35857-39-7
CMF C10 H8 F3 N5



CM 2

CRN 130-85-8
CMF C23 H16 O6



L21 ANSWER 64 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1972:113258 CAPLUS Full-text
DOCUMENT NUMBER: 76:113258
TITLE: 6-(Fluoro and trifluoromethyl phenyl)-3,5-diamino-1,2,4-triazines and substituted-6-phenylalkyl-3,5-diamino-1,2,4-triazines
INVENTOR(S): Rees, Richard W.; Russell, Peter B.
PATENT ASSIGNEE(S): American Home Products Corp.
SOURCE: U.S., 3 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 3637688	A	19720125	US 1970-1842	19700109 <--
GB 1318645	A	19730531	GB 1970-43096	19700909 <--
PRIORITY APPLN. INFO.:			US 1970-1842 A	19700109 <--

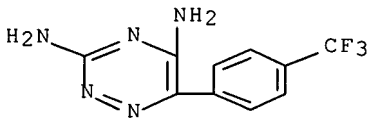
GI For diagram(s), see printed CA Issue.

AB -F3CC6H4-COCN was treated with H2NC(:NH)NHNH2 and HNO3 and the product cyclized with KOH to give a title triazine (I, R = p-F3CC6H4). Five I (R = m-F3CC6H4, p-FC6H4, 0-FC6H4, 3,5-(F3C)2C6H3, PhCMe2) were similarly prepared I were antimalarial.

IT 35857-39-7P 35857-40-0P 35857-41-1P
35857-42-2P 35857-43-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

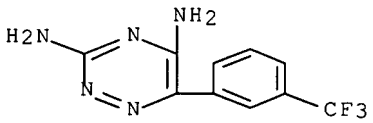
RN 35857-39-7 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



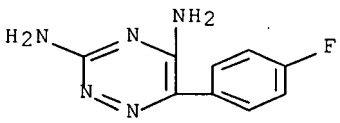
RN 35857-40-0 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



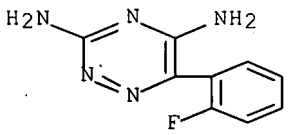
RN 35857-41-1 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(4-fluorophenyl)- (9CI) (CA INDEX NAME)

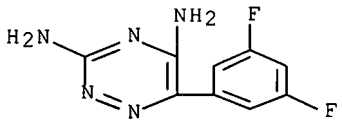


RN 35857-42-2 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



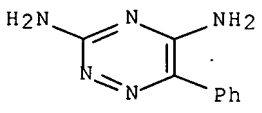
RN 35857-43-3 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(3,5-difluorophenyl)- (9CI) (CA INDEX NAME)



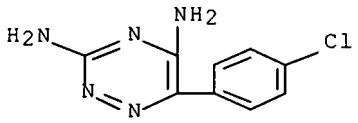
L21 ANSWER 65 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1968:104123 CAPLUS Full-text
DOCUMENT NUMBER: 68:104123
ORIGINAL REFERENCE NO.: 68:20079a,20082a
TITLE: Effects of chemosterilants and growth regulators on the pea aphid fed an artificial diet
AUTHOR(S): Bhalla, O. P.; Robinson, Arthur Grant
CORPORATE SOURCE: Univ. Manitoba, Winnipeg, Can.
SOURCE: Journal of Economic Entomology (1968), 61(2), 552-5
CODEN: JEENAI; ISSN: 0022-0493
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Nymphs of the pea aphid, Acyrthosiphon pisum, were fed on synthetic liquid diets containing chemosterilants or growth regulators. Mortality and fecundity were measured for effects of 27 chemosterilants, maleic hydrazide, Cycocel (2-chloroethyl)trimethylammonium chloride), and synthetic "queen substance" (trans-9-oxodec-2-enoic acid). At specified dosages, 6 of the chemosterilants caused permanent sterility, 2 caused temporary sterility, and 21 decreased fecundity. Both maleic hydrazide and synthetic "queen substance" caused high mortality to feeding nymphs, and reduced fecundity in surviving adults. Cycocel was not as toxic to feeding nymphs, but adult fecundity was reduced.

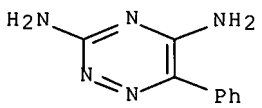
IT 6719-24-0
RL: BIOL (Biological study)
(pea aphid control by, as sterilant)
RN 6719-24-0 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-phenyl- (9CI) (CA INDEX NAME)



L21 ANSWER 66 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:429460 CAPLUS Full-text
DOCUMENT NUMBER: 65:29460
ORIGINAL REFERENCE NO.: 65:5461b-c
TITLE: Heterocyclic amines. A convenient synthesis of 3,5-diamino-1,2,4-triazine derivatives
AUTHOR(S): Settepani, Joseph A.; Borkovec, A. B.
SOURCE: Journal of Heterocyclic Chemistry (1966), 3(2), 188-90
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 65:29460
AB A facile synthesis of 3,5-diamino-1,2,4-triazines via condensations in acidic media of acylnitriles with aminoguanidine and subsequent base-catalyzed cyclization of the resulting acylnitrile amidinohydrazones is described.
IT 6662-28-8P, as-Triazine, 3,5-diamino-6-(p-chlorophenyl)-
6719-24-0P, as-Triazine, 3,5-diamino-6-phenyl-
RL: PREP (Preparation)
(preparation of)
RN 6662-28-8 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(4-chlorophenyl)- (9CI) (CA INDEX NAME)



RN 6719-24-0 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-phenyl- (9CI) (CA INDEX NAME)



L21 ANSWER 67 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1962:483316 CAPLUS Full-text
DOCUMENT NUMBER: 57:83316
ORIGINAL REFERENCE NO.: 57:16638a-d
TITLE: Novel hydrazine derivatives
PATENT ASSIGNEE(S): F. Hoffmann-La Roche & Co., A.-G.
SOURCE: 7 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

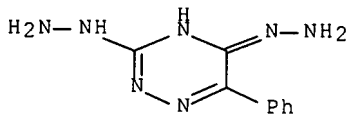
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 881340		19611101	GB 1960-18648	19600526 <--
US 3077473		19630212	US 1960-31274	19600524 <--
PRIORITY APPLN. INFO.:			FR	19590528 <--

AB Hydrazinotriazines were prepared as potential vasodilators. Thus, 0.5 mole Et glyoxylate was added to a solution of 0.5 mole thiosemicarbazide in 450 ml. H2O, prepared at 60-70°, the mixture kept overnight in the refrigerator, the precipitated Et glyoxylate thiosemicarbazone (I) centrifuged off, and an addnl. quantity recovered by concentrating the filtrate to half its volume in vacuo, m. 170-1° (decomposition). I (0.1 mole) was dissolved in 300 ml. N NaOH, refluxed 1 hr., cooled, acidified in the cold with concentrated HCl, concentrated to half the volume in vacuo, kept overnight in the refrigerator and the product 5-hydroxy-3-mercapto-1,2,4-triazine (II) dried, m. 248-50° (decomposition). II (0.1 mole) was dissolved in 150 ml. of 2N NaOH, 0.11 mole MeI added, agitated, until homogeneous for 30 min., acidified in the cold with concentrated HCl, kept overnight in a refrigerator and the product 5-hydroxy-3-methylthio-1,2,4-triazine (III) centrifuged and dried, m. 213-15°. III (8 g.) in 80 ml. alc. were refluxed 4 hrs. with 18 ml. of 50% NH2NH2, cooled, centrifuged, washed with a very small amount of H2O, recrystd. from H2O, decolorized with animal charcoal and filtered to yield the product 3-hydrazino-5-hydroxy-1,2,4-triazine, m. 248-50° (decomposition). Similarly 3-hydrazino-5-hydroxy-1,2,4-triazine- 6-carboxylic acid, m. 300° (H2O); 3,5-dihydrazino-6-ethyl-1,2,4- triazine, m. 165° 3,5-dihydrazino-6-phenyl-1,2,4-triazine, m. 175° (decomposition); 3,5-dihydrazino-6-benzyl-1,2,4-triazine, m. 102-3° (soften and decomposition); 3,5-dihydrazino-1,2,4-triazine, m. 220-1° (decomposition); 3,5-dihydrazino-6-methyl-1,2,4-triazine, m. 218-20° (decomposition); 3,5-dihydrazino-6-propyl-1,2,4-triazine, m. 117-18° (decomposition) (MeOH); 3,5-dihydrazino-6-heptyl-1,2,4triazine, m. 70-80° (decomposition) (MeOH); 3,5-dihydrazino-6-isopropyl-1,2,4- triazine-HCl, m. 230° (decomposition).

IT 70997-61-4P, as-Triazine, 3,5-dihydrazino-6-phenyl-
RL: PREP (Preparation)
(preparation of)

RN 70997-61-4 CAPLUS

CN 1,2,4-Triazine-3,5(2H,4H)-dione, 6-phenyl-, dihydrazone (9CI) (CA INDEX NAME)



L21 ANSWER 68 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1961:93517 CAPLUS Full-text
DOCUMENT NUMBER:	55:93517
ORIGINAL REFERENCE NO.:	55:17644h-i,17645a-d
TITLE:	New asymmetric triazines
AUTHOR(S):	Libermann, David; Jacquier, Robert
SOURCE:	Bulletin de la Societe Chimique de France (1961) 383-90 CODEN: BSCFAS; ISSN: 0037-8968
DOCUMENT TYPE:	Journal
LANGUAGE:	Unavailable
OTHER SOURCE(S):	CASREACT 55:93517

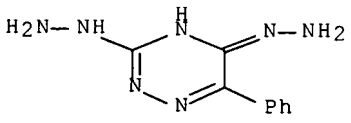
GI For diagram(s), see printed CA Issue.

AB Heating N:N.C(SH):N.C(OH):CR (I) or N:N.C(SH):N.C(SH):CR (II) with excess N2H4 in EtOH gave N:N.C(NHNH2):N.C(OH):CR (III) or N:N.C(NHNH2):N.C(NHNH2):CR (IV), resp. Yields were improved by prior methylation of the SH groups in I and II. I derivs. were prepared by cyclization of thiosemicarbazones of α-oxo acids in NaOH. In the preparation of II the hydroxyl group in I was replaced by heating with P2S5. Infrared spectra of the solid II compds. in Nujol indicated they were in the dithioxo form, and showed no -SH absorption in the region 2600-2550 cm.-1 Introduction of alkyl substituents in the 6-position of IV increased hypotensive activity beginning with Et, but the activity decreased with excessive chain length. Aromatic groups in the 6-position of IV increased toxicity. Data given for the starting α-oxo acid thiosemicarbazones, RC(CO2R'):NNHCONH2, were R, R', and m.p., resp.: H, Et, 170-1°; CO2H, H, 223-5°; Et, H, 172-3°; Pr, H, 164-5°; iso-Pr, H, 170-2°; n-C7H15, H, 121-3°. Given for I compds. were R, m.p., % yield, and λEtOH in mμ (log ε), resp.: H, 248-50°, 74.4-80.6, 271 (4.23); Me, 215-16°, 80, 215 (4.01) 272.5 (4.33); Et, 166-7°, 83, 214 (4.01) 272.5 (4.28); CO2H, 223-5°, 80, -; CO2Et, 207-9°, 75, -; Pr, 149-50°, .apprx.87, -; iso-Pr, 215-16°, 33, -; n-C7H15, 135-6°, .apprx.84, -; PhCH2, 188-90°, -, 272 (4.34); Ph, 258-9°, -, 225 (3.98) 283 (4.45) 344 (4.05). Given for II were R, m.p., % yield, λEtOH in mμ (log ε), resp.: H, 225-6° (decomposition), .apprx.100, 283 (4.44) 321 (4.07); Me, 215-17°, .apprx.100, 281.5 (4.42) 321.5 (4.13); Et, 185-6°, 90, 282 (4.48) 321 (4.11); Pr, 160-2, 90, -; iso-Pr, 226-8°, 85, -; n-C7H15, 122-3°, 50, -; PhCH2, 181-2°, 80, 284 (4.49) 325 (4.10); Ph, 234-5°, 94, 290 (4.53). Dimethylated derivs. of II include R = H, m. 56-7°, and R = Me, m. 75-6°. The partially reacted product, 3-methylthio-5-hydrazino-6-methyl-1,2,4- triazine, m. 168-70°. Given for N:N.C(SMe):N.C(OH):CR were R, m.p., and % yield, resp.: H, 213-15°, 75; Me, 223-5°, 85; CO2H, 213-15°, 75. Similarly for III were: H, 248-50° (decomposition), 55; Me, 240-2° (decomposition), 90; CO2H (N2H4 salt), >300°, 78. Given for IV were R, m.p. (decomposition), % yield, resp.: H, 210-12°, 70; Me, 218-20°, 72; Et, 165-7°, 85; Pr, 117-18°, 60; iso-Pr (HCl salt), 230°, 15; n-C7H15, 70-80°, 15; PhCH2, 102-3° (with 1 mole MeOH), 54; Ph, 175-80°, 32.

IT 70997-61-4P, as-Triazine, 3,5-dihydrazino-6-phenyl-
RL: PREP (Preparation)
(preparation of)

RN 70997-61-4 CAPLUS

CN 1,2,4-Triazine-3,5(2H,4H)-dione, 6-phenyl-, dihydrazone (9CI) (CA INDEX NAME)



L21 ANSWER 69 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1959:79063 CAPLUS Full-text

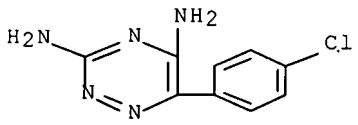
DOCUMENT NUMBER: 53:79063

ORIGINAL REFERENCE NO.: 53:14345g-i

TITLE: Metabolism of human leucocytes in vitro. H. Effect of several agents on the incorporation of radioactive formate and glycine

AUTHOR(S): Winzler, Richard J.; Wells, Warren; Shapira, Jacob; Williams, Albert D.; Bornstein, Irene; Burr, Mary J.;

Best, Wm. R.
CORPORATE SOURCE: Univ. of Illinois, Chicago
SOURCE: Cancer Research (1959), 19, 377-87
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C.A. 52, 476f; 53, 4512g. Chronic granulocytic leukemia leucocytes exhibited the greatest incorporation of radioglycine; normal leucocytes incorporated the least, while chronic lymphocytic leukemia cells had an intermediate activity. The compds. most effective in influencing formate incorporation were purine riboside, amethopterin, Daraprim, and triazine, the last 3 affecting chronic granulocytic leukemia cells particularly. Azaserine and 6-diazo-5-oxo-L-norleucine at high concentration affected all types of cells, and Chlorambucil was unique in causing a profound stimulation of formate uptake by normal and chronic lymphocytic leukemia cells. Purine riboside also exerted an appreciable but nonselective inhibition of glycine incorporation, while the folic acid antagonists had little or no effect on the uptake of this isotope. Azaserine profoundly affected glycine incorporation into chronic lymphocytic leukemia cells and produced a lesser inhibition with chronic granulocytic leukemia and normal cells. No correlation between clinical and in vitro effects of chemotherapeutic agents used in the treatment of leukemia could be drawn from this study.
IT 6662-28-8, as-Triazine, 3,5-diamino-6-(p-chlorophenyl)-
(effect on formate and glycine incorporation in leucocytes)
RN 6662-28-8 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(4-chlorophenyl)- (9CI) (CA INDEX NAME)



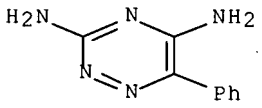
L21 ANSWER 70 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1959:72677 CAPLUS
DOCUMENT NUMBER: 53:72677
ORIGINAL REFERENCE NO.: 53:13186d-g
TITLE: 3,5-Diamino-6-phenyl-1,2,4-triazines
INVENTOR(S): Hitchings, Geo. H.; Russell, Peter B.; Maggiolo, Allison D.
PATENT ASSIGNEE(S): Wellcome Foundation Ltd.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 951996		19561108	DE	<--

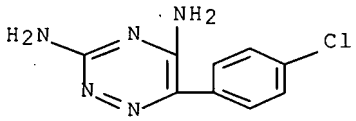
AB 3,5-Diamino-6-phenyl-1,2,4-triazines are prepared by converting the 5-hydroxy group of 3-alkylthio-5-hydroxy-6-phenyl-1,2,4-triazine(alkyl = Me, Et, or Pr) to the 5-Cl compound with POCl3 and treating the 5-chlorotriazine with NH3. Et phenylglyoxylate (20 g.) and 15 g. thiosemicarbazide is dissolved in 350 ml. 50% aqueous alc., 2 ml. AcOH added, and the mixture heated to a clear solution and kept overnight to give 15 g. thiosemicarbazone of Et phenylglyoxylate (I), m. 144-5°. I in 225 ml. 1:2 EtOH-benzene is heated 1

hr. with 5 g. NaOMe in MeOH, evaporated, acidified with AcOH, and diluted with H2O to yield 6.5 g. 4-mercapto-5-hydroxy-6-phenyl-1,2,4-triazine (II), m. 257-8° (EtOH). II (10.2 g.) in 200 ml. alc. kept 3 hrs. with 1.2 g. NaOH and 10 g. MeI, refluxed 2 hrs., diluted with H2O, and acidified gave 10 g. 3-methylthio-5-hydroxy-6-phenyl-1,2,4-triazine (III), m. 235-6° (EtOH). III (7.5 g.) is refluxed 1 hr. with 80 ml. POCl3, evaporated, the residue dissolved in 100 ml. CHCl3, poured on ice, and made alkaline with NH4OH with vigorous stirring. After 30 min. the CHCl3 layer is washed twice with H2O) and the CHCl3 distilled The residue heated 16 hrs. with 100 ml. saturated EtOH-NH3 at 150-70° in closed vessel, the solvent distilled, the residue treated with concentrated NaOH solution, and the solid filtered off gives 3,5-diamino-6-phenyl-1,2,4-triazine as needles, m. 206° aqueous(alc.).

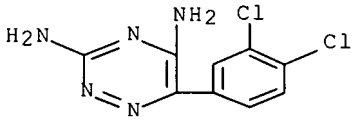
IT 6719-24-0, as-Triazine, 3,5-diamino-6-phenyl-
(and derivs.)
RN 6719-24-0 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-phenyl- (9CI) (CA INDEX NAME)



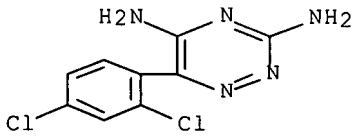
IT 6662-28-8P, as-Triazine, 3,5-diamino-6-(p-chlorophenyl)-
36518-85-1P, as-Triazine, 3,5-diamino-6-[3,4-dichlorophenyl]-
38943-76-9P, as-Triazine, 3,5-diamino-6-[2,4-dichlorophenyl]-
RL: PREP (Preparation)
(preparation of)
RN 6662-28-8 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(4-chlorophenyl)- (9CI) (CA INDEX NAME)



RN 36518-85-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(3,4-dichlorophenyl)- (9CI) (CA INDEX NAME)



RN 38943-76-9 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,4-dichlorophenyl)- (9CI) (CA INDEX NAME)



L21 ANSWER 71 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1957:52183 CAPLUS
DOCUMENT NUMBER: 51:52183
ORIGINAL REFERENCE NO.: 51:9719a-f
TITLE: Triazines
PATENT ASSIGNEE(S): Burroughs, Wellcome & Co. (U.S.A.) Inc.; Wellcome Foundation Ltd.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

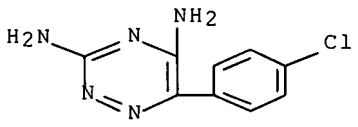
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
GB 759014		19561010	GB		<--

GI For diagram(s), see printed CA Issue.

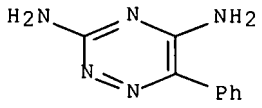
AB N:N.CR:N.CR':CR'' (I), having growth-inhibitory properties as well as antimalarial activity, are described. BzCO2Et (II) (20 g.) and 15 g. H2NCSNHNH2 (III) in 350 ml. 50% aqueous EtOH treated with 2 ml. AcOH, boiled on a hot plate until all had dissolved, then boiled an addnl. hr., and allowed to stand overnight gave 15 g. II thiosemicarbazone (IV), m. 144-5°. IV (10 g.) dissolved in 225 ml. of 1:2 (volume/volume) EtOH-C6H6, 5 g. NaOMe added, heating continued 1 hr., the solution concentrated to a small volume, acidified with AcOH, diluted with water, and the precipitate (6.5 g.) filtered off and recrystd. from EtOH gave I (R = HS, R' = HO, R'' = Ph) (V),m. 257-8°. A cool solution of 10.2 g. V and 1.2 g. NaOH in 200 ml. EtOH treated with 10 g. MeI, allowed to stand 3 hrs., refluxed 2 hrs., diluted with water, acidified, and the precipitate (10 g.) recrystd. from EtOH gave I (R = MeS, R' = HO, R'' = Ph) (VI), m. 235-6°. Alternatively, VI was prepared as follows. II (20 g.) in 200 ml. EtOH treated with 25 g. H2NC(SMe):NNH2.HCl and 10 ml. AcOH, refluxed 3 hrs. on a steam bath, cooled, 20 g. NaOAc and 12 g. NaOMe added with stirring, and the solution (pH 7) diluted with 250 ml. water, heated 2 hrs. more, and acidified, gave VI, m. and mixed m.p. 235-6°. VI (7.5 g.) refluxed with 80 ml. POCl3 until the solution was evaporated, the residue dissolved in 100 ml. CHCl3, poured on cracked ice, made alkaline with NH4OH solution with strong stirring, the CHCl3 layer separated after 30 min., washed twice with H2O, the CHCl3 evaporated, the semicryst. residue heated 16 hrs. at 150-70° in a sealed tube with 100 ml. saturated alc. NH3, the EtOH and excess NH3 evaporated, and the residue treated with strong NaOH solution and recrystd. from aqueous EtOH gave I (R = R' = H2N, R'' = Ph), needles, m. 206°. Similarly were prepared the following I (R, R', R'', m.p. given): HS, HO, p-ClC6H4, 284° (from aqueous EtOH) [from p-ClC6H4COCO2Me, m. 60-1° (from Et2O-petr. ether), giving with III the thiosemicarbazide, m. 152°, which was then cyclized]; MeS, HO, p-ClC6H4, 280-2° (from aqueous EtOH); H2N, H2N, p-ClC6H4, 218-20° (from aqueous EtOH); HS, HO, 2,4-Cl2C6H3, 219-20° (from C6H6) (from 2,4-Cl2C6H3COCO2Me and III followed by ring closure); MeS, HO, 2,4-Cl2C6H3, 250-3° (from aqueous EtOH); H2N, H2N, 2,4-Cl2C6H3 220-2° (from aqueous EtOH); HS, HO, 3,4-Cl2C6H3, 227-30° (from C6H6-EtOH) (from 3,4-Cl2C6H3COCO2Me and III, followed by ring closure); MeS, HO, 3,4-Cl2C6H3, 272-80° (from aqueous EtOH); H2N, H2N, 3,4-Cl2C6H3, 219-20° (from aqueous EtOH).

IT 6662-28-8P, as-Triazine, 3,5-diamino-6-(p-chlorophenyl)-
6719-24-0P, as-Triazine, 3,5-diamino-6-phenyl- 36518-85-1P
, as-Triazine, 3,5-diamino-6-[3,4-dichlorophenyl]- 38943-76-9P,
as-Triazine, 3,5-diamino-6-[2,4-dichlorophenyl]-
RL: PREP (Preparation)
(preparation of)

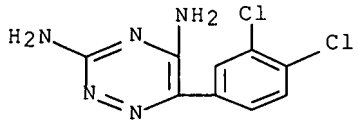
RN 6662-28-8 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(4-chlorophenyl)- (9CI) (CA INDEX NAME)



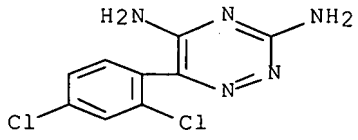
RN 6719-24-0 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-phenyl- (9CI) (CA INDEX NAME)



RN 36518-85-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(3,4-dichlorophenyl)- (9CI) (CA INDEX NAME)



RN 38943-76-9 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,4-dichlorophenyl)- (9CI) (CA INDEX NAME)



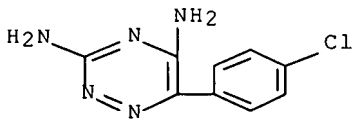
L21 ANSWER 72 OF 72 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1954:14783 CAPLUS Full-text
DOCUMENT NUMBER: 48:14783

ORIGINAL REFERENCE NO.: 48:2719h-i
TITLE: 3,5-Diamino-as-triazines as inhibitors of lactic acid bacteria and plasmodia
AUTHOR(S): Hitchings, G. H.; Maggiolo, A.; Russell, P. B.; Werff, H. Vander; Rollo, I. M.
CORPORATE SOURCE: Wellcome Research Labs., Tuckahoe, NY
SOURCE: Journal of the American Chemical Society (1952), 74, 3200-1
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB cf. Falco, et al., C.A. 46, 4675b. The following compds. were prepared: 3,5-diamino-1-(p-bromophenyl)-1H-1,2,4-triazole, m. 210°; 3,5-diamino-6-(3,4-dichlorophenyl)-as-triazine, m. 219-20°; 6-(p-chlorophenyl) analog, m. 218-20°. The relation between antifolic acid activity, antimalarial activity, and chemical structure is discussed.

IT 6662-28-8, as-Triazine, 3,5-diamino-6-(p-chlorophenyl)-
36518-85-1, as-Triazine, 3,5-diamino-6-(3,4-dichlorophenyl)-
(as antimalarial and folic acid antagonist)

RN 6662-28-8 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(4-chlorophenyl)- (9CI) (CA INDEX NAME)



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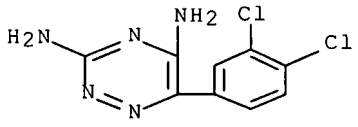

1408 REFERENCES FOR THIS SINGLE COMPOUND (ONLY the oldest 9 are displayed):

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L12        1408 SEA FILE=CAPLUS ABB=ON  PLU=ON  L10


=> d l12 ibib abs hitstr 1400-1408

L12  ANSWER 1400 OF 1408  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         1988:112505  CAPLUS  Full-text
DOCUMENT NUMBER:          108:112505
TITLE:                    Preparation of 3,5-diamino-6-(2,3-dichlorophenyl)-
                          1,2,4-triazine isethionate as an antiepileptic
INVENTOR(S):              Sawyer, David Alan; Copp, Frederick Charles
PATENT ASSIGNEE(S):       Wellcome Foundation Ltd., UK
SOURCE:                   Eur. Pat. Appl., 5 pp.
                          CODEN: EPXXDW
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
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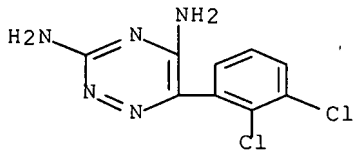
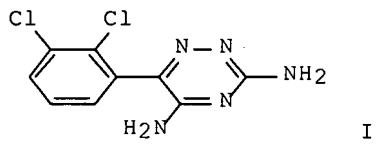
     EP 247892             A1    19871202    EP 1987-304776           19870529
     EP 247892             B1    19910424
         R:  AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE
     DK 8702759            A     19871201    DK 1987-2759             19870529
     DK 166278             B     19930329
     DK 166278             C     19930823
     FI 8702406            A     19871201    FI 1987-2406             19870529
     FI 90770              B     19931215
     FI 90770              C     19940325
     AU 8773684            A     19871203    AU 1987-73684            19870529
     AU 597982             B2    19900614
     JP 62289570           A     19871216    JP 1987-134772           19870529
     JP 07051571           B     19950605
     HU 45978              A2    19880928    HU 1987-2487             19870529
     HU 196769             B     19890130
     ZA 8703896            A     19890125    ZA 1987-3896             19870529
     US 4847249            A     19890711    US 1987-56136            19870529
     AT 62902              T     19910515    AT 1987-304776           19870529
     CA 1286670            C     19910723    CA 1987-538395           19870529
     IL 82710              A     19920115    IL 1987-82710            19870529
PRIORITY APPLN. INFO.:                       GB 1986-13183       A    19860530
                                             EP 1987-304776      A    19870529
AB   The title compound (I.isethionate), useful as an anticonvulsant (no data), was
     prepared by reaction of I with 2-hydroxyethanesulfonic acid (II) or by
     reaction of I salts with the anion of II.  A 1.0 M solution of Na isethionate
     in H2O was passed through a column of IR 120 (H) ion exchange resin.  I
     (preparation given) was added to the resulting II and the solution was
     filtered and evaporated  Recrystn. from industrial methylated spirit gave 72%
     I.isethionate.
IT   84057-84-1P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation and conversion of, into isethionate salt)
RN   84057-84-1  CAPLUS
```

CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (CA INDEX NAME)



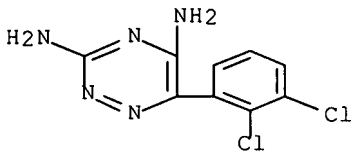
L12 ANSWER 1401 OF 1408 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:48658 CAPLUS Full-text
DOCUMENT NUMBER: 108:48658
TITLE: Lamotrigine, a new anticonvulsant: pharmacokinetics in normal humans
AUTHOR(S): Cohen, A. F.; Land, G. S.; Breimer, D. D.; Yuen, W. C.; Winton, C.; Peck, A. W.
CORPORATE SOURCE: Clin. Appl. Res. Div., Wellcome Res. Lab., Beckenham/Kent, BR3 3BS, UK
SOURCE: Clinical Pharmacology & Therapeutics (St. Louis, MO, United States) (1987), 42(5), 535-41
CODEN: CLPTAT; ISSN: 0009-9236
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



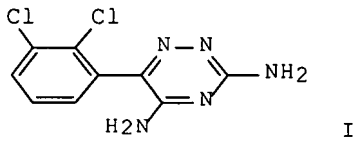
I

AB The pharmacokinetics of lamotrigine (I), a new anticonvulsant, were studied in 3 studies in normal volunteers. In the 1st study, subjects received oral doses of lamotrigine ≤ 240 mg. A linear relationship was observed between dose administration and both peak drug concentration and area under the concentration curve. In a 2nd study 10 subjects received 120 mg lamotrigine and the mean of the elimination half-life (t1/2) was 24.1 h and of volume of distribution/bioavailability 1.2 L/kg. Saliva concns. were 46% of the plasma concentration Total urinary recovery of drug over 144 h was 70.5% of the oral dose. A glucuronide conjugate accounted for 89.4% of the urinary recovery. In a third study the kinetics of repeated administration were studied. Fifteen subjects were randomized to lamotrigine or placebo and received multiple doses over 7 days. The overall plasma elimination t1/2 calculated from data during the 7 days was 25.5 h. Observed pharmacokinetics on multiple administration obeyed closely those predicted from the single-dose experiment, suggesting the absence of autoinduction of metabolism No clin. important side effects or changes in central nervous system or cardiovascular system variables, hematol., biochem., or urinalysis occurred during the 7 days.

IT 84057-84-1, Lamotrigine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pharmacokinetics of, in human)
RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (CA INDEX NAME)

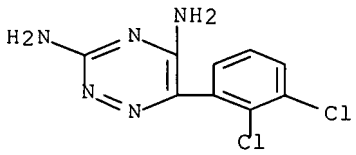


L12 ANSWER 1402 OF 1408 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:15 CAPLUS Full-text
DOCUMENT NUMBER: 106:15
TITLE: Lamotrigine [pharmacology]
AUTHOR(S): Miller, A. A.; Sawyer, D. A.; Roth, B.; Peck, A. W.; Leach, M. J.; Wheatley, P. L.; Parsons, D. N.; Morgan, R. J. I.
CORPORATE SOURCE: Wellcome Res. Lab., Beckenham/Kent, BR3 3BS, UK
SOURCE: Current Problems in Epilepsy (1986), 4(New Anticonvulsant Drugs), 165-77
CODEN: CPEPES; ISSN: 0950-4591
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
GI



I

AB A review, with 16 refs., of the pharmacol. of the anticonvulsant drug lamotrigine (I) [84057-84-1].
IT 84057-84-1, Lamotrigine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. of, in humans and laboratory animals)
RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (CA INDEX NAME)

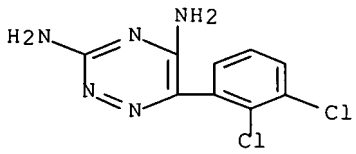


L12 ANSWER 1403 OF 1408 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:603145 CAPLUS Full-text
DOCUMENT NUMBER: 105:203145
TITLE: Pharmacological studies on lamotrigine, a novel potential antiepileptic drug: II. Neurochemical studies on the mechanism of action
AUTHOR(S): Leach, Michael J.; Marden, Caroline M.; Miller, Alistair A.
CORPORATE SOURCE: Dep. Pharmacol., Wellcome Res Lab., Beckenham/Kent, BR3 3BS, UK
SOURCE: Epilepsia (1986), 27(5), 490-7
CODEN: EPILAK; ISSN: 0013-9580
DOCUMENT TYPE: Journal
LANGUAGE: English

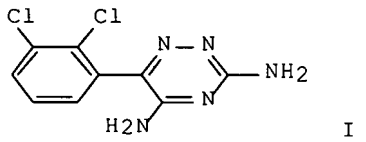
AB The effect of lamotrigine (LTG) [84057-84-1] was compared with that of phenytoin, on the release of endogenous amino acids and radiolabeled acetylcholine [51-84-3] evoked by veratrine or K, from slices of rat cerebral cortex in vitro. Both veratrine and K evoked a marked release of glutamate [56-86-0] and γ-aminobutyric acid (GABA) [56-12-2], with a more moderate release of aspartate [56-84-8]. LTG inhibited veratrine-evoked release of glutamate and aspartate, with ED50 values of 21 μM for both amino acids, but LTG was less potent in the inhibition of GABA release (ED50 = 44 μM). At concns. up to 300 μM, LTG had no effect on K-evoked amino acid release of on spontaneous release. Also, LTG was some 5-times less potent in the inhibition of veratrine-evoked [3H]acetylcholine release (ED50 = 100 μM), than in glutamate or aspartate release. The total lack of effect of LTG on K-evoked release and the potent effect on veratrine-evoked release (at concns. found in rat brain after anticonvulsant doses) strongly suggest that LTG acts at voltage-sensitive Na channels to stabilize neuronal membranes and inhibit transmitter release, principally glutamate. The role of glutamate in the etiol. of epilepsy is discussed.

IT 84057-84-1
RL: BIOL (Biological study)
(acetylcholine and endogenous amino acids release response to, in cerebral cortex, antiepileptic mechanism in relation to)

RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (CA INDEX NAME)



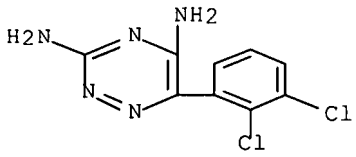
L12 ANSWER 1404 OF 1408 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:603144 CAPLUS Full-text
DOCUMENT NUMBER: 105:203144
TITLE: Pharmacological studies on lamotrigine, a novel potential antiepileptic drug: I. Anticonvulsant profile in mice and rats
AUTHOR(S): Miller, Alistair A.; Wheatley, Philip; Sawyer, David A.; Baxter, Martin G.; Roth, Barbara
CORPORATE SOURCE: Dep. Pharmacol., Wellcome Res. Lab., Beckenham/Kent, BR3 3BS, UK
SOURCE: Epilepsia (1986), 27(5), 483-9
CODEN: EPILAK; ISSN: 0013-9580
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



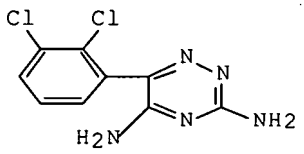
I

AB Lamotrigine (LTG)(I) [84057-84-1] is a structurally novel anticonvulsant. The anticonvulsant profile of LTG following oral administration in 2 standard anticonvulsant tests, the maximal electroshock (MES) test in mice and rats and the pentylenetetrazol (PTZ) infusion test in mice, was studied in comparison with the known anticonvulsant drugs phenytoin (PHT), phenobarbitone, diazepam, carbamazepine (CBZ), sodium valproate, ethosuximide (ETH), and troxidone (TROX). ED50 values for the abolition of hindlimb extension (HLE) in the MES test and PTZ infusion tests and doses increasing the latency of PTZ-evoked clonus were determined The duration of action of LTG was examined in rats and mice in the MES test by determining ED50 values for the abolition of HLE at various drug intervals to shock administration. In the MES test, LTG was well absorbed in both species, with peak activity at 1 h and persistence at this level of potency for at least 8 h. Of the drugs examined, LTG was ranked the most potent and persistent in both species. LTG also abolished PTZ-evoked HLE, while ETH and TROX were inactive. Clonus latency was not increased by LTG, PHT, or CBZ, but was increased by the remaining anticonvulsants. Thus, LTG resembled PHT and CBZ in its ability to block HLE but not to increase PTZ-induced clonus latency. Acute behavioral studies in mice and rats suggested a wide separation between anticonvulsant doses and those producing behavioral impairment. These results suggest that LTG may be of value in the treatment of generalized tonic-clonic and partial seizures.

IT 84057-84-1
RL: PRP (Properties)
(anticonvulsant profile and behavior effects of)
RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (CA INDEX NAME)



L12 ANSWER 1405 OF 1408 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:102360 CAPLUS Full-text
DOCUMENT NUMBER: 104:102360
TITLE: Lamotrigine (BW430C), a potential anticonvulsant. Effects on the central nervous system in comparison with phenytoin and diazepam
AUTHOR(S): Cohen, A. F.; Ashby, L.; Crowley, D.; Land, G.; Peck, A. W.; Miller, A. A.
CORPORATE SOURCE: Wellcome Res. Lab., Beckenham/Kent, UK
SOURCE: British Journal of Clinical Pharmacology (1985), 20(6), 619-29
CODEN: BCPHBM; ISSN: 0306-5251
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

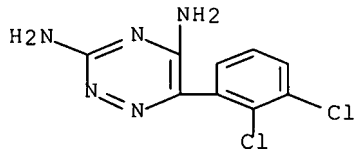


I

AB Healthy male volunteers received phenytoin [57-41-0] 0.5 and 1 g, lamotrigine (I) [84057-84-1] (a new anticonvulsant) 120 and 240 mg, diazepam [439-14-5] 10 mg and placebo orally in a double-blind, cross-over, randomized trail. Maximum drug concns. at 4 h, measured in plasma were 11.5 μg/mL for phenytoin and 2.7 μg/mL for lamotrigine. These levels were in the therapeutic range for phenytoin and the putative therapeutic range for lamotrigine. Side effects after diazepam (mainly sedation) and phenytoin (mainly unsteadiness) differed markedly from lamotrigine which produced no important side effects. Subjective effects as measured by visual analog scales were caused by phenytoin and diazepam but not by lamotrigine. Diazepam impaired eye movements, adaptive tracking and body sway. Phenytoin impaired adaptive tracking, increased body sway and impaired smooth pursuit eye movement. Lamotrigine produced only a possible slight increase in body sway. There were significant correlations between performance and saliva levels of phenytoin and diazepam. The tests used were suitable for monitoring central nervous system (CNS) effects of anticonvulsants and lamotrigine possibly could have a more favorable CNS side effect than phenytoin.

IT 84057-84-1
RL: BIOL (Biological study)
(central nervous system response to, in human)

RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (CA INDEX NAME)



L12 ANSWER 1406 OF 1408 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1985:542021 CAPLUS Full-text
DOCUMENT NUMBER: 103:142021
TITLE: Triazine compounds having cardiovascular activity
INVENTOR(S): Allan, Geoffrey; Miller, Alastair Ainslie; Sawyer, David Alan
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 142306	A2	19850522	EP 1984-307374	19841026
EP 142306	A3	19861120		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4649139	A	19870310	US 1984-663682	19841022
DK 8405121	A	19850428	DK 1984-5121	19841026
FI 8404212	A	19850428	FI 1984-4212	19841026
AU 8434758	A	19850509	AU 1984-34758	19841026
AU 564667	B2	19870820		
JP 60109577	A	19850615	JP 1984-225636	19841026
DD 224033	A5	19850626	DD 1984-268757	19841026
HU 36102	A2	19850828	HU 1984-4003	19841026
HU 191566	B	19870330		
ES 537104	A1	19860416	ES 1984-537104	19841026
ZA 8408388	A	19860625	ZA 1984-8388	19841026
SU 1371500	A3	19880130	SU 1984-3805251	19841026
IL 73332	A	19880630	IL 1984-73332	19841026
PL 144899	B1	19880730	PL 1984-250213	19841026
CA 1261328	A1	19890926	CA 1984-466473	19841026

PRIORITY APPLN. INFO.: GB 1983-28757 A 19831027
OTHER SOURCE(S): MARPAT 103:142021
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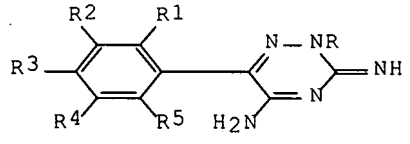


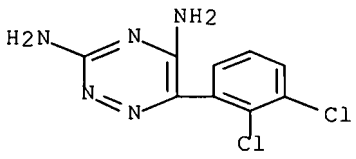
I

AB Tautomeric iminotriazinamines I [R = (un)substituted C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, C3-10 cycloalkyl; R1-R5 = H, halogen, alkenyloxy, acyl, acyloxy, cyano, NO2, aryl, alkylthio, (un)substituted alkyl, alkenyl, alkynyl, alkoxy, amino; R1R2, R2R3, R3R4, R4R5 = CH:CHCH:CH] were prepared Thus, 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine was alkylated with Me2CHI to give I-HI (R = Me2CH, R1 = R2 = Cl; R3-R5 = H) which was converted to the mesylate salt (II) (12% overall yield). II at 1 mg/kg i.v. to rats increased the amount of aconitine required to elicit ventricular arrhythmias by 490% compared with 84% for 1 mg/kg verapamil.

IT 84057-84-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and N-alkylation of)

RN 84057-84-1 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (CA INDEX NAME)



L12 ANSWER 1407 OF 1408 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1983:89397 CAPLUS Full-text

DOCUMENT NUMBER: 98:89397

TITLE: Substituted aromatic compounds

INVENTOR(S): Baxter, Martin G.; Elphick, Albert R.; Miller, Alistair A.; Sawyer, David A.

PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK

SOURCE: Can., 26 pp. Division of Can. Appl. No. 353,081.
CODEN: CAXXA4

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 1133938	A2	19821019	CA 1981-373126	19810316
CA 1112643	A1	19811117	CA 1980-353081	19800530
US 4486354	A	19841204	US 1981-308805	19811005
AU 566870	B2	19871105	AU 1983-14051	19830428
US 4602017	A	19860722	US 1984-583286	19840227
FI 8400888	A	19840306	FI 1984-888	19840306
FI 73203	B	19870529		
FI 73203	C	19870910		

PRIORITY APPLN. INFO.:

GB 1979-19257	A	19790601
CA 1980-353081	A3	19800530
US 1980-154198	A1	19800529
FI 1980-1758	A	19800530
CA 1981-373126		19810316

US 1981-302365 A1 19810915

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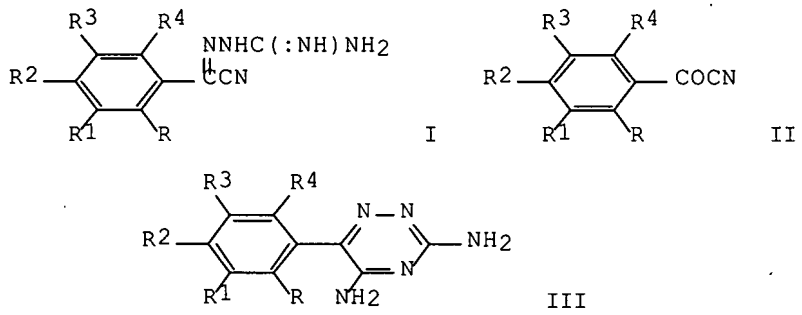
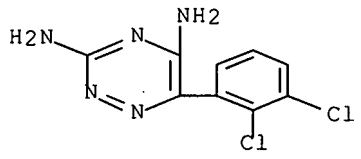


AB [(Cyanobenzylidene)amino]guanidines I (R-R4 = H, halo, alkyl, F3C; RR1 = HC:CHCH:CH, halobenzo, trifluoromethylbenzo, alkylbenzo) were prepared from the benzoyl cyanides II and H2NNHC(:NH)NH2 and were useful as intermediates in the preparation of anticonvulsant triazines III. Thus, 2,3-Cl2C6H3COCl was treated with CuCN to give 2,3-Cl2C6H3COCN which was treated with H2NNHC(:NH)NH2 to give I (R = R1 = Cl, R2 = R3 = R4 = H), which was cyclized by KOH to give III (R = R2 = Cl, R2 = R3 = R4 = H) (IV). The anticonvulsant ED50 of IV was 2.4 mg/kg in the maximal electroshock test.

IT 84057-84-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and anticonvulsant activity of)

RN 84057-84-1 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (CA INDEX NAME)



L12 ANSWER 1408 OF 1408 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1981:208914 CAPLUS Full-text

DOCUMENT NUMBER: 94:208914

TITLE: 1,2,4-Triazine derivatives, pharmaceutical compositions and intermediates utilized for their preparation

INVENTOR(S): Baxter, Martin George; Elphick, Albert Reginald; Miller, Alistair Ainslie; Sawyer, David Alan

PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK

SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 21121	A1	19810107	EP 1980-103032	19800530
EP 21121	B1	19830511		
R: BE, CH, DE, FR, GB, LU, NL, SE				
DK 8002338	A	19801202	DK 1980-2338	19800530
DK 153787	B	19880905		
DK 153787	C	19890116		
FI 8001758	A	19801202	FI 1980-1758	19800530
FI 67844	B	19850228		
FI 67844	C	19850610		
AU 8058906	A	19801204	AU 1980-58906	19800530
AU 530999	B2	19830804		
JP 56025169	A	19810310	JP 1980-71580	19800530
JP 01044706	B	19890929		
ES 491998	A1	19810516	ES 1980-491998	19800530
DD 151309	A5	19811014	DD 1980-221474	19800530
ZA 8003250	A	19820127	ZA 1980-3250	19800530
AT 8002896	A	19820715	AT 1980-2896	19800530
AT 370097	B	19830225		
EP 59987	A1	19820915	EP 1982-102293	19800530
EP 59987	B1	19850814		
R: BE, CH, DE, FR, GB, LU, NL, SE				
PL 124029	B1	19821231	PL 1980-224633	19800530
HU 24621	A2	19830328	HU 1980-1364	19800530
HU 182086	B	19831228		
IL 60201	A	19840531	IL 1980-60201	19800530
CS 234018	B2	19850314	CS 1980-3829	19800530
SU 1055331	A3	19831115	SU 1980-2932704	19800602
US 4486354	A	19841204	US 1981-308805	19811005
US 4602017	A	19860722	US 1984-583286	19840227
FI 8400888	A	19840306	FI 1984-888	19840306
FI 73203	B	19870529		
FI 73203	C	19870910		
JP 61033163	A	19860217	JP 1985-121370	19850604
JP 01044179	B	19890926		

PRIORITY APPLN. INFO.:
GB 1979-19257 A 19790601
US 1980-154198 A1 19800529
EP 1980-103032 A 19800530
FI 1980-1758 A 19800530
US 1981-302365 A1 19810915

OTHER SOURCE(S): MARPAT 94:208914
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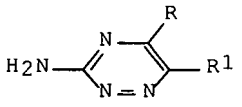


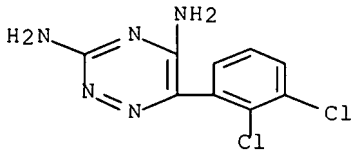
I

AB Triazines I (R = NH2, acylamino, aminomethyleneamino; R1 = substituted Ph) were prepared Thus, 2,3-Cl2C6H3I was Grignard carboxlated and the 2,3-Cl2C6H3CO2H converted to the chloride and treated with CuCN to give 2,3-Cl2C6H3COCN which was cyclized with aminoguanidine bicarbonate to I (R = NH2, R1 = 2,3-Cl2C6H3). The latter compound had an anticonvulsant ED50 of 2.4 mg/kg orally in mice.

IT 84057-84-1P
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation, acetylation and anticonvulsant activity of)

RN 84057-84-1 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (CA INDEX NAME)



INVENTOR NAME SEARCH:

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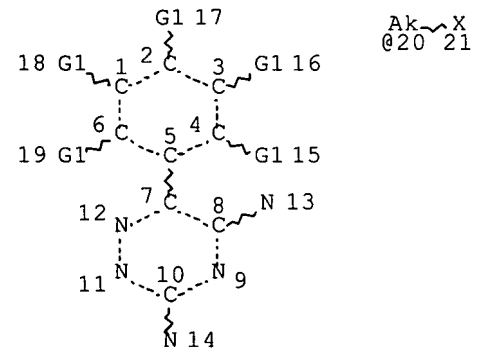


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  21

STEREO ATTRIBUTES: NONE
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L22  ANSWER 1 OF 13  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2006:918809  CAPLUS  Full-text
DOCUMENT NUMBER:          145:306838
TITLE:                    Treatment of cytokine dysregulation by using sn-2
```

gamma-linolenoyl, gamma-dihomolinolenoyl or arachidonoyl patty acid glycerol monoesters
INVENTOR(S): Harbige, Laurence S.; Leach, Michael J.; Barraclough, Paul
PATENT ASSIGNEE(S): Btg International Limited, UK
SOURCE: PCT Int. Appl., 44pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006092622	A1	20060908	WO 2006-GB778	20060302

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2005-4333 A 20050302

AB A method of treating a patient in need of therapy for a cytokine dysregulation comprising administering to that patient a therapeutically ED of a monoglyceride or metabolic precursor formula (I, HOCH2CH(OR1)CH2OH) wherein R1 = fatty acyl group of an essential poyunsatd. fatty acid selected from γ-linolenoyl, γ-dihomolinolenoyl and arachidonoyl. A method for the preparation of the glycerides of the invention is also disclosed. Treatment of multiple sclerosis patients with high sn-2 γ-linolenoyl acid resulted in increased peripheral blood mononuclear cell production of TGFβ-1 and decrease in TNFα and IL-β1.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:918700 CAPLUS Full-text
DOCUMENT NUMBER: 145:306860
TITLE: Cyclic glycerides of essential polyunsatd. fatty acids as cytokine modulators for neurol. diseases
INVENTOR(S): Harbige, Laurence S.; Leach, Michael J.; Barraclough, Paul; Dolan, Anthony Patrick
PATENT ASSIGNEE(S): Btg International Limited, UK
SOURCE: PCT Int. Appl., 44pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006092623	A1	20060908	WO 2006-GB779	20060302

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

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GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
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KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.: GB 2005-4362 A 20050302
OTHER SOURCE(S): MARPAT 145:306860
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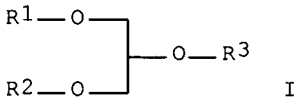

I

AB A method of treating a patient in need of therapy for a cytokine dysregulation comprising administering to that patient a therapeutically ED of a compound of formula (I) where R1 and R2 together form a group -(CH2)n-CR4R5-(CH2)m- wherein n and m are independently selected integers 0, 1 or 2 and R4 and R5 are independently selected from H, C1-18 alkyl, C1-18alkoxy, C1-18n hydroxyalkyl, C2-18 alkenyl and C6-18aryl or aralykyl and R3 is the a fatty acyl group of an essential polyunsatd. fatty acid. A method for the preparation of the compds. of this invention is disclosed.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:513564 CAPLUS Full-text
DOCUMENT NUMBER: 145:21213
TITLE: Structured phospholipids
INVENTOR(S): Harbige, Laurence S.; Leach, Michael J.; Sharief, Mohammed; Barraclough, Paul
PATENT ASSIGNEE(S): BTG International Limited, UK
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006056783	A2	20060601	WO 2005-GB4516	20051125
WO 2006056783	A3	20070301		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
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GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
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MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,

SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, S, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2004-25932 A 20041125
OTHER SOURCE(S): MARPAT 145:21213

AB A method of treating a patient in need of therapy for a disease in which cytokines have become dysregulated, or are otherwise capable of modulation to provide therapeutic benefit, is provided comprising administering to that patient a therapeutically ED of a phospholipid comprising a phosphatidyl group esterified with one or more fatty acyl groups, characterized in that the phospholipid has at least one fatty acyl group at the sn-1 and/or sn-2 position of the phosphatidyl group, the fatty acyl group being selected from the group consisting of γ-linolenoyl, dihomo-γ-linolenoyl acid and arachidonoyl. Particularly is provided a method for modulating transforming growth factor β (TGF-β), particularly TGF-β1, but also cytokines TNF-α and IL-1β, still more preferably for maintaining and/ or restoring cytokine balance where imbalance is found in diseases of the immune system and in neurodegeneration. Such diseases include multiple sclerosis and various autoimmune states.

L22 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:43151 CAPLUS Full-text
DOCUMENT NUMBER: 144:226149
TITLE: A novel drug binding site on voltage-gated sodium channels in rat brain
AUTHOR(S): Riddall, Dieter R.; Leach, Michael J.; Garthwaite, John
CORPORATE SOURCE: Wolfson Institute for Biomedical Research, University College London, London, UK
SOURCE: Molecular Pharmacology (2006), 69(1), 278-287
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

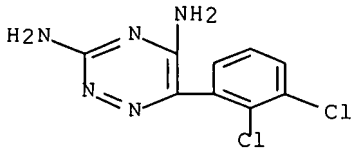
AB The effectiveness of several antiepileptic, analgesic, and neuroprotective drugs is attributable to state-dependent inhibition of voltage-gated sodium channels. To help characterize their site and mode of action on sodium channels, a member of the lamotrigine family, R-(-)-2,4-diamino-6-(fluoromethyl)-5-(2,3,5-trichlorophenyl)-pyrimidine (BW202W92), was radiolabeled and used as a binding ligand in rat forebrain synaptosomes. Although the level of specific [3H]BW202W92 binding in a standard incubation medium was relatively poor, low concns. of tetrodotoxin (EC50 = 2-3 nM) greatly enhanced the binding, apparently by increasing the affinity of the binding sites. Tetrodotoxin-dependent binding was stereoselective (the less active enantiomer, S-(-)-2,4-diamino-6-(fluoromethyl)-5-(2,3,5-trichlorophenyl)-pyrimidine (BW203W92), was up to 30-fold less potent, depending on conditions) and was extremely sensitive to inhibition by raised K+ concentration (IC50 = 5.9 mM), an effect that was ascribed to changes in membrane potential. In addition, the binding was inhibited by sodium channel neurotoxins acting on sites 3 and 4, but it was resistant to batrachotoxin (site 2) and brevetoxin (site 5). Several drugs acting on sodium channels displaced tetrodotoxin-dependent [3H]BW202W92 binding, and most of those tested showed different affinities under depolarized (100 mM K+) and polarized

(1 mM K+) conditions. In a subset of compds. for which data were available, binding affinity in depolarized synaptosomes correlated well with apparent affinity for the inactivated state of sodium channels. The [3H]BW202W92 binding site is novel and is likely to represent a pharmacol. important site of action of drugs on voltage-gated sodium channels in the brain.

IT 84057-84-1, Lamotrigine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel drug binding site on voltage-gated sodium channels in rat brain)

RN 84057-84-1 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:177887 CAPLUS Full-text
DOCUMENT NUMBER: 142:274043
TITLE: Glycerides containing γ-linolenic acid, dihomo-γ-linolenic acid or arachidonic acid in the sn-2 position for the treatment of neurodegenerative conditions
INVENTOR(S): Harbige, Laurence S.; Leach, Michael J.; Sharief, Mohammed; Barraclough, Paul
PATENT ASSIGNEE(S): BTG International Limited, UK
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005018632	A1	20050303	WO 2004-GB3524	20040813
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004266480	A1	20050303	AU 2004-266480	20040813
CA 2534202	A1	20050303	CA 2004-2534202	20040813

EP 1660071	A1	20060531	EP 2004-768085		20040813
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR					
DE 112004001520	T5	20060706	DE 2004-112004001520		20040813
GB 2422373	A	20060726	GB 2006-3646		20040813
CN 1867328	A	20061122	CN 2004-80030644		20040813
JP 2007502805	T	20070215	JP 2006-523678		20040813
FI 2006000154	A	20060217	FI 2006-154		20060217
NO 2006001232	A	20060515	NO 2006-1232		20060317
PRIORITY APPLN. INFO.:			GB 2003-19358	A	20030818
			GB 2004-10846	A	20040514
			WO 2004-GB3524	W	20040813

OTHER SOURCE(S): CASREACT 142:274043; MARPAT 142:274043

AB A method is provided for treating a patient in need of therapy for a neurodegenerative disease comprising administering to that patient a therapeutically ED of a lipid glyceride comprising a glycerol moiety and a fatty acid moiety, the fatty acid moiety being selected from the group consisting of γ-linolenic acid, dihomo-γ-linolenic acid and arachidonic acid characterized in that the selected fatty acid moiety is attached to the glycerol moiety at its sn-2 position. Preferably, the lipid is administered for a duration and at a dose sufficient to maintain or elevate TGF-β1 levels in the patient to therapeutic levels. A method for preparation of the glycerides of the invention is also disclosed.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1015873 CAPLUS Full-text
DOCUMENT NUMBER: 141:420459
TITLE: Use of triglyceride oils containing γ-linolenic acid residues and linoleic acid residues for the treatment of neurodegenerative disease
INVENTOR(S): Harbige, Laurence S.; Leach, Michael J.; Sharief, Mohammed
PATENT ASSIGNEE(S): BTG International Limited, UK
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004100943	A1	20041125	WO 2004-GB2089	20040514
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004237936	A1	20041125	AU 2004-237936	20040514
CA 2524036	A1	20041125	CA 2004-2524036	20040514
GB 2415378	A	20051228	GB 2005-21395	20040514

GB 2415378	B	20060802			
EP 1631280	A1	20060308	EP 2004-733020		20040514
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DE 112004000762	T5	20060330	DE 2004-112004000762		20040514
JP 2006528233	T	20061214	JP 2006-530503		20040514
CN 1901898	A	20070124	CN 2004-80012982		20040514
SE 2005002484	A	20060116	SE 2005-2484		20051110
FI 2005001280	A	20060207	FI 2005-1280		20051213
NO 2005005937	A	20051214	NO 2005-5937		20051214
PRIORITY APPLN. INFO.:			GB 2003-11081	A	20030514
			US 2003-497332P	P	20030825
			WO 2004-GB2089	W	20040514

OTHER SOURCE(S): MARPAT 141:420459

AB A method is provided for treating a patient in need of therapy for a neurodegenerative disease, comprising administering a therapeutically ED of a triglyceride oil containing both γ-linolenic acid and linoleic acid residues as triglyceride ester, the ratio of γ-linolenic acid to linoleic acid residues at the sn-2 position of the triglyceride being at least 0.8; the amount of γ-linolenic acid residues at the sn-2 position being at least 18%, wherein the oil is administered at a dose sufficient to maintain or elevate TGF-β1 levels in the patient at a therapeutic level. Preferably the method is that wherein the therapeutic level is such as to produce a TGF-β1/TNF-α ratio of at least 0.5 in blood of a patient after 18 mo of daily dosing. Preferred oils are Borage or Mucor oils having at least 35% of the sn-2 position fatty acid residues as γ-linolenic acid.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:999675 CAPLUS Full-text

DOCUMENT NUMBER: 141:406127

TITLE: Lamotrigine and related compounds for the treatment of multiple sclerosis

INVENTOR(S): Harbige, Laurence S.; Leach, Michael J.; Sharief, Mohammed

PATENT ASSIGNEE(S): BTG International Limited, UK

SOURCE: U.S. Pat. Appl. Publ., 4 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004229873	A1	20041118	US 2004-756761		20040114
PRIORITY APPLN. INFO.:			GB 2003-783	A	20030114

OTHER SOURCE(S): MARPAT 141:406127

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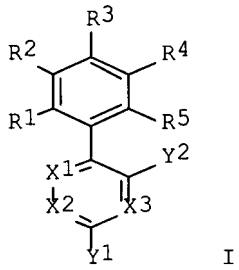


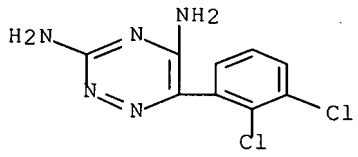
I

AB A method of treating a patient in need of therapy for multiple sclerosis is provided, comprising administering a therapeutically ED of I [R1-R5 = H, trihaloalkyl, halo; X1-X3 = CH, CCH2F, CCF3, COalkyl, CCH3, N (with proviso); Y1, Y2 = H, primary amino, secondary amino, tertiary amino] during periods of remission, as well as during relapse. Preferred compds. include e.g. lamotrigine and sipatrigine. The therapy results in reduction of one or more of incidence of relapse, spasticity and fatigue and exceptionally the therapy stabilizes the patients Expanded Disability Status Score (EDSS), thus halting progress of the disease.

IT 84057-84-1, Lamotrigine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lamotrigine and related compds. for treatment of multiple sclerosis)

RN 84057-84-1 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (CA INDEX NAME)



L22 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:492216 CAPLUS Full-text

DOCUMENT NUMBER: 125:159224

TITLE: Vicious cycle involving Na+ channels, glutamate release, and NMDA receptors mediates delayed neurodegeneration through nitric oxide formation

AUTHOR(S): Strijbos, Paul J. L. M.; Leach, Michael J.; Garthwaite, John

CORPORATE SOURCE: Neurosci. Res., Wellcome Res. Lab., Beckenham, Kent, BR3 3BS, UK

SOURCE: Journal of Neuroscience (1996), 16(16), 5004-5013
CODEN: JNRSDS; ISSN: 0270-6474

PUBLISHER: Society for Neuroscience

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The mechanisms by which neurons die after cerebral ischemia and related conditions in vivo are unclear, but they are thought to involve voltage-

dependent Na+ channels, glutamate receptors, and nitric oxide (NO) formation because selective inhibition of each provides neuroprotection. It is not known precisely what their roles are, nor whether they interact within a single cascade or in parallel pathways. These questions were investigated using an in vitro primary cell culture model in which striatal neurons undergo a gradual and delayed neurodegeneration after a brief (5 min) challenge with the glutamate receptor agonist NMDA. Unexpectedly, NO was generated continuously by the cultures for up to 16 h after the NMDA exposure. Neuronal death followed the same general time course except that its start was delayed by .apprx.4 h. Application of the NO synthase inhibitor nitroarginine after, but not during, the NMDA exposure inhibited NO formation and protected against delayed neuronal death. Blockade of NMDA receptors or of voltage-sensitive Na+ channels [with tetrodotoxin (TTX)] during the postexposure period also inhibited both NO formation and cell death. The NMDA exposure resulted in a selective accumulation of glutamate in the culture medium during the period preceding cell death. This glutamate release could be inhibited by NMDA antagonism or by TTX, but not by nitroarginine. These data suggest that Na+ channels, glutamate receptors, and NO operate interdependently and sequentially to cause neurodegeneration. At the core of the mechanism is a vicious cycle in which NMDA receptor stimulation caused activation of TTX-sensitive Na+ channels, leading to glutamate release and further NMDA receptor stimulation. The output of the cycle is an enduring production of NO from neuronal sources, and this is responsible for delayed neuronal death. The same neurons, however, could be induced to undergo more rapid NMDA receptor-dependent death that required neither TTX- sensitive Na+ channels nor NO.

L22 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:95416 CAPLUS Full-text
DOCUMENT NUMBER: 120:95416
TITLE: BW619C89, a glutamate release inhibitor, protects against focal cerebral ischemic damage
AUTHOR(S): Leach, M. J.; Swan, J. H.; Eisenthal, D.; Dopson, M.; Nobbs, M.
CORPORATE SOURCE: Dep. Pharmacol., Wellcome Res. Lab., Beckenham/Kent, BR3 3BS, UK
SOURCE: Stroke (1993), 24(7), 1063-7
CODEN: SJCCA7; ISSN: 0039-2499
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The excitatory amino acid neurotransmitter glutamate is involved in excitotoxic brain injury and neurodegeneration after cerebral ischemia. Therefore, compds. that block the release of glutamate may be useful as cerebroprotective agents. The purpose of this study was to evaluate the cerebroprotective properties of a glutamate release inhibitor, BW619C89. In the studies reported here, the effect of BW619C89 [4-amino-2-(4-methyl-1-piperazinyl)-5-(2,3,5-trichlorophenyl)pyrimidine] on neurotransmitter release (endogenous amino acids, γ-aminobutyric acid, and acetylcholine) from slices of rat brain cerebral cortex in vitro was determined The neuroprotective efficacy of BW619C89 was evaluated using the middle cerebral artery occlusion model of focal cerebral ischemia in the Fischer 344 rat. In the in vitro studies, BW619C89 inhibited veratrine- (but not K-) evoked release of both endogenous glutamate and aspartate from rat cerebral cortex slices with IC50 values of approx. 5 μM. BW619C89 was .apprx.10-fold less potent to inhibit veratrine-evoked 3H-γ-aminobutyric acid release (IC50=51 μM), 4-fold less potent to inhibit 3H-acetylcholine release (IC50=21 μM), and at 10 μM had only weak activity at excitatory amino acid (N-methyl-D-aspartate, kainate, and α-amino-3-hydroxy-5-methyl-4- isoxazolepropionic acid) binding sites. When administered i.v. to Fischer 344 rats 5 min after permanent middle cerebral

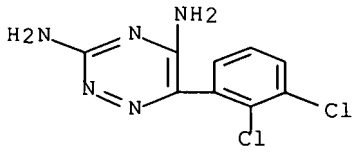
artery occlusion, BW619C89 produced marked redns. of both total (cortex and basal ganglia) and cortical infarct vols. Cortical infarct size was reduced by 20% at a dose of BW619C89 of 5 mg/kg (n=6, not significant); 43% at 10 mg/kg (n=8, P<.01); 59% at 20 mg/kg (n=8, P<.001); 61% at 30 mg/kg (n=8, P<.001), and 53% at 40 mg/kg (n=8, P<.001). BW619C89 at doses of 20 and 30 mg/kg also reduced noncortical (basal ganglia) infarct vols., demonstrating that a proportion of this tissue also appears to be salvageable. Behavioral effects observed were dose related, generally minor, and at doses of 20 mg/kg IV and above consisted of body tremor and mild ataxia lasting .apprx.2 h. Probably glutamate release inhibitors such as BW619C89 may provide an alternative to excitatory amino acid receptor antagonists in the treatment of focal cerebral ischemia and stroke.

L22 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:531450 CAPLUS Full-text
DOCUMENT NUMBER: 119:131450
TITLE: Studies on the mechanism of action of the novel anticonvulsant lamotrigine (Lamictal) using primary neuroglial cultures from rat cortex
AUTHOR(S): Lees, George; Leach, Michael J.
CORPORATE SOURCE: Dep. Pharmacol., Wellcome Res. Lab., Beckenham/Kent, BR3 3BS, UK
SOURCE: Brain Research (1993), 612(1-2), 190-9
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English

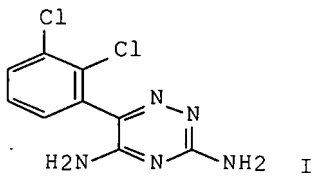
AB Whole cell and perforated patch clamp expts. were conducted on cultured cortical rat neurons (7-21 days in vitro) in order to determine the effects of the anticonvulsant and glutamate release inhibitor lamotrigine (10-100 μM), on CNS receptors and ion channels. The compound inhibited, indiscriminately, both excitatory and inhibitory synaptic events which occurred spontaneously in cultured neural circuits. The drug did not mimic diazepam as a pos. modulator of GABAA currents. In the presence of tetrodotoxin, voltage-gated potassium currents and composite currents evoked by L-glutamate were not significantly modulated even at the highest dose. Unitary, fast, presumptive-sodium spikes, evoked at low frequencies, were not blocked significantly by lamotrigine. In contrast, burst firing induced by pulsed application of L-glutamate or potassium ions was markedly depressed at 10 μM. Presumptive calcium currents were inhibited by lamotrigine at 100 μM. It is proposed that the drug inhibits epileptiform burst firing preferentially by state/activity dependent interactions with voltage and gated cation channels. Potential mechanisms for inhibition of glutamate release are discussed.

IT 84057-84-1, Lamotrigine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, mechanism of, in cerebral cortex neurons, glutamate release and ion channels in)

RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (CA INDEX NAME)

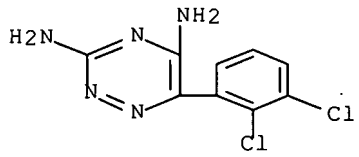


L22 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:207638 CAPLUS Full-text
DOCUMENT NUMBER: 116:207638
TITLE: Neurochemical and behavioral aspects of lamotrigine
AUTHOR(S): Leach, M. J.; Baxter, M. G.; Critchley, M. A. E.
CORPORATE SOURCE: Dep. Pharmacol., Wellcome Res. Lab., Beckenham/Kent, UK
SOURCE: Epilepsia (1991), 32(Suppl. 2), S4-8
CODEN: EPILAK; ISSN: 0013-9580
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

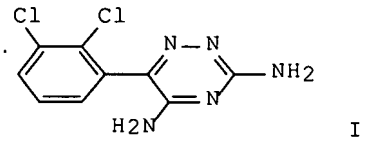


I

AB Lamotrigine (LTG, I), a new anticonvulsant, chemical unrelated to current antiepileptic drugs (AEDs), resembles phenytoin (PHT) and carbamazepine (CBZ) in ability to block hindlimb extension in both the maximal electroshock test and leptazol-induced seizures. Results indicate that LTG may be of value in both partial and generalized seizures. In in vitro studies, LTG has been shown to inhibit veratrine-evoked release of glutamate when a threshold depolarizing concentration (4 μg/mL) is used, and also inhibits aspartate release when a larger stimulus is given (10 μg/mL). However, LTG does not block potassium-evoked transmitter release. LTG is a less potent inhibitor of the release of γ-aminobutyric acid (GABA), acetylcholine, noradrenaline, and dopamine. LTG blocks the neurotoxicity of kainic acid in vivo, supporting the in vitro findings, and suggests that the anticonvulsant effect of LTG may be due to inhibition of glutamate release. In a test of working memory and phencyclidine (PCP) discrimination studies, LTG had no effect, indicating no sharing of the same PCP-like side effects associated with NMDA receptor blockade. In the gerbil model of global ischemia, high doses of LTG provided protection against damage to the CA1 region of the hippocampus. Analogs of LTG of higher potency to block the release of glutamate may be necessary to ensure protection against ischemic brain damage.
IT 84057-84-1, Lamotrigine
RL: PRP (Properties)
(neurochem. and behavioral effects of)
RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (CA INDEX NAME)

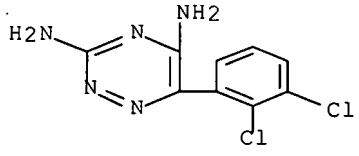


L22 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:15 CAPLUS Full-text
DOCUMENT NUMBER: 106:15
TITLE: Lamotrigine [pharmacology]
AUTHOR(S): Miller, A. A.; Sawyer, D. A.; Roth, B.; Peck, A. W.; Leach, M. J.; Wheatley, P. L.; Parsons, D. N.; Morgan, R. J. I.
CORPORATE SOURCE: Wellcome Res. Lab., Beckenham/Kent, BR3 3BS, UK
SOURCE: Current Problems in Epilepsy (1986), 4(New Anticonvulsant Drugs), 165-77
CODEN: CPEPES; ISSN: 0950-4591
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
GI



I

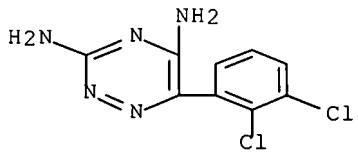
AB A review, with 16 refs., of the pharmacol. of the anticonvulsant drug lamotrigine (I) [84057-84-1].
IT 84057-84-1, Lamotrigine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. of, in humans and laboratory animals)
RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (CA INDEX NAME)



L22 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:603145 CAPLUS Full-text
DOCUMENT NUMBER: 105:203145
TITLE: Pharmacological studies on lamotrigine, a novel potential antiepileptic drug: II. Neurochemical studies on the mechanism of action
AUTHOR(S): Leach, Michael J.; Marden, Caroline M.; Miller, Alistair A.
CORPORATE SOURCE: Dep. Pharmacol., Wellcome Res Lab., Beckenham/Kent, BR3 3BS, UK
SOURCE: Epilepsia (1986), 27(5), 490-7
CODEN: EPILAK; ISSN: 0013-9580
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of lamotrigine (LTG) [84057-84-1] was compared with that of phenytoin, on the release of endogenous amino acids and radiolabeled acetylcholine [51-84-3] evoked by veratrine or K, from slices of rat cerebral cortex in vitro. Both veratrine and K evoked a marked release of glutamate [56-86-0] and γ-aminobutyric acid (GABA) [56-12-2], with a more moderate release of aspartate [56-84-8]. LTG inhibited veratrine-evoked release of glutamate and aspartate, with ED50 values of 21 μM for both amino acids, but LTG was less potent in the inhibition of GABA release (ED50 = 44 μM). At concns. up to 300 μM, LTG had no effect on K-evoked amino acid release of on spontaneous release. Also, LTG was some 5-times less potent in the inhibition of veratrine-evoked [3H]acetylcholine release (ED50 = 100 μM) than in glutamate or aspartate release. The total lack of effect of LTG on K-evoked release and the potent effect on veratrine-evoked release (at concns. found in rat brain after anticonvulsant doses) strongly suggest that LTG acts at voltage-sensitive Na channels to stabilize neuronal membranes and inhibit transmitter release, principally glutamate. The role of glutamate in the etiol. of epilepsy is discussed.

IT 84057-84-1
RL: BIOL (Biological study)
(acetylcholine and endogenous amino acids release response to, in cerebral cortex, antiepileptic mechanism in relation to)
RN 84057-84-1 CAPLUS
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (CA INDEX NAME)



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                OR "LEACH MIKE"/AU)
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                "SHARIEF M K"/AU OR "SHARIEF MOHAMMAD K"/AU OR "SHARIEF
                MOHAMMED"/AU OR "SHARIEF MOHAMMED K"/AU)
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L18           7 SEA ABB=ON  PLU=ON  L16 AND ?NEURODEGEN?
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